EMS MEDICAL DIRECTOR: James E. Pointer, MD, FACEP DATE: May 16, 2000

LOCAL EMS AGENCY: Alameda County Emergency Medical Services

NAME OF PROPOSED PROCEDURE OR MEDICATION: Amiodarone HCl

1. DESCRIPTION OF THE PROCEDURE OR MEDICATION REQUESTED:

   Amiodarone HCl, Intravenous

2. DESCRIPTION OF THE MEDICAL CONDITIONS FOR WHICH THEY WILL BE UTILIZED:

   Pulseless ventricular fibrillation/ventricular tachycardia refractory to electrical defibrillation.
   May increase mortality in MI.

3. ALTERNATIVES (Please describe any alternate therapies considered for the same condition and any advantages and disadvantages):

	ADVANTAGES	DISADVANTAGES
Lidocaine	Long-time use; current drug of choice	No improvement in survival; Class II B
Bretylium	Long-time use	No improvement in survival; Not currently available
Procaineamide	Long-time use	No improvement in survival; Class II B; Also requires action by Scope Committee

4. PATIENT POPULATION THAT WOULD BENEFIT, INCLUDING AN ESTIMATE OF FREQUENCY OF UTILIZATION:

   V Fib/ V Tach cardiac arrests refractory to defibrillation; approximately 300 patients/year

5. OTHER FACTORS OR EXCEPTIONAL CIRCUMSTANCES:

   1 - Inclusion of amiodarone in 2000 ACLS ventricular fibrillation protocols is imminent.
   2 - At least ten other EMS agencies/providers have begun using amiodarone (attached).
   3 - Amiodarone is the only available agent to improve survival to hospital admission from ventricular fibrillation cardiac arrest.

6. ANY SUPPORTING DATA, INCLUDING RELEVANT STUDIES AND MEDICAL LITERATURE.

   See attached.

7. RECOMMENDED POLICIES/PROCEDURES TO BE INSTITUTED REGARDING USE, MEDICAL CONTROL, TREATMENT PROTOCOLS, AND QUALITY ASSURANCE OF THE PROCEDURE OR MEDICATION.

   See attached.

8. DESCRIPTION OF THE TRAINING AND COMPETENCY TESTING REQUIRED TO IMPLEMENT THE PROCEDURE OR MEDICATION.

   See attached.

Supporting Data, Including Relevant Studies, and Medical Literature

RELEVANT STUDIES

EFFICACY TO CONVERT VENTRICULAR ARRHTHYMIAS

1. Bretylium's use may be limited by high incidence of hypotension (See Kowey, et al.)

2. Amiodarone is effective in treating life-threatening tachyarrhythmias (See Scheinman, et al.)

3. Amiodarone and bretylium have comparable efficacies in the treatment of malignant ventricular arrhythmias (See Kowey, et al.)

SURVIVAL/MORTALITY STUDIES

1. Lidocaine may adversely affect MI mortality rates (See Sadowski, et al.)

2. ACLS drugs do not improve resuscitation from in-hospital cardiac arrest (See van Walraven, et al.)

3. Lidocaine, when compared to ACLS without lidocaine, fails to increase survival in out-of-hospital patients with refractory ventricular fibrillation arrest (See Harrison)

4. Epinephrine and lidocaine did not improve outcome in patients in ventricular fibrillation cardiac arrest (See Weaver, et al.)

5. Lidocaine, compared to epinephrine, associated with higher incidence of post defibrillation asystole (See Weaver, et al.)

6. Amiodarone increases survival to ED in out-of-hospital patients with ventricular fibrillation arrest (See Kudenchuk, et al.)

Do Advanced Cardiac Life Support Drugs Increase Resuscitation Rates From In-Hospital Cardiac Arrest?

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Presented at the Annual Meeting of the Society for Academic Emergency Medicine, Washington DC, May 19–22, 1997.

Part of this study was completed while Dr van Walraven was an R Samuel McLaughlin Research Fellow.

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Study objective: The benefit of Advanced Cardiac Life Support (ACLS) medications during cardiac resuscitation is uncertain. The objective of this study was to determine whether the use of these medications increased resuscitation from in-hospital cardiac arrest.

Methods: A prospective cohort of patients undergoing cardiac arrest in 1 of 5 academic hospitals was studied. Patient and arrest factors related to resuscitation outcome were recorded. We determined the association of the administration of ACLS drugs (epinephrine, atropine, bicarbonate, calcium, lidocaine, and bretylium) with survival at 1 hour after resuscitation.

Results: Seven hundred seventy-three patients underwent cardiac resuscitation, with 269 (34.8%) surviving for 1 hour. Use of epinephrine, atropine, bicarbonate, calcium, and lidocaine was associated with a decreased chance of successful resuscitation ($P<.001$ for all except lidocaine, $P<.01$). While controlling for significant patient factors (age, gender, and previous cardiac or respiratory disease) and arrest factors (initial cardiac rhythm, and cause of arrest), multivariate logistic regression demonstrated a significant association between unsuccessful resuscitation and the use of epinephrine (odds ratio .08 [95% confidence interval .04–.14]), atropine (.24 [.17–.35]), bicarbonate (.31 [.21–.44]), calcium (.32 [.18–.55]), and lidocaine (.48 [.33–.71]). Drug effects did not improve when patients were grouped by their initial cardiac rhythm. Cox proportional hazards models that controlled for significant confounders demonstrated that survivors were significantly less likely to receive epinephrine ($P<.001$) or atropine ($P<.001$) throughout the arrest.

Conclusion: We found no association between standard ACLS medications and improved resuscitation from in-hospital cardiac arrest. Randomized clinical trials are needed to determine whether other therapies can improve resuscitation from cardiac arrest when compared with the presently used ACLS drugs.

[van Walraven C, Stiell IG, Wells GA, Hébert PC, Vandemheen K, for the OTAC Study Group: Do Advanced Cardiac Life Support

secondary to co-intervention. Second, the number of patients surviving to hospital discharge was small, thereby limiting any analysis. Finally, if no association between a medication and successful resuscitation at 1 hour exists, it is unlikely that survival to discharge would be changed by the medication.

Data analysis

The association of each ACLS medication with survival to 1 hour was determined by describing drug administration as given or not (using the χ^2 test) and as the time to drug administration (using Student *t* test). To determine each drug's association with resuscitation outcome while controlling for potentially significant confounding variables, multivariate logistic regression using model-building strategies suggested by Kleinbaum et al[11] was used. Confounding variables were defined as those with a significant ($P<.1$) univariate association with resuscitation outcome and were included in the logistic models. Logistic models did not show changes in the association of each drug with resuscitation outcome when either standard or ACD-CPR was used.[10] We did not model other specific interactions because we wanted to attain an overall estimate of each drug's effect adjusted for the confounders.[11] To identify subgroups that would benefit from the drugs, these models were repeated grouping patients by their initial cardiac rhythm.

Cox proportional hazards analysis was used to compare the proportion of survivors and nonsurvivors who received each medication by each minute of the resuscitation. For each drug, we modeled time to drug administration (dependent variable) while controlling for all significant confounders (independent variables) and grouping patients by survival status (stratifying variable). These

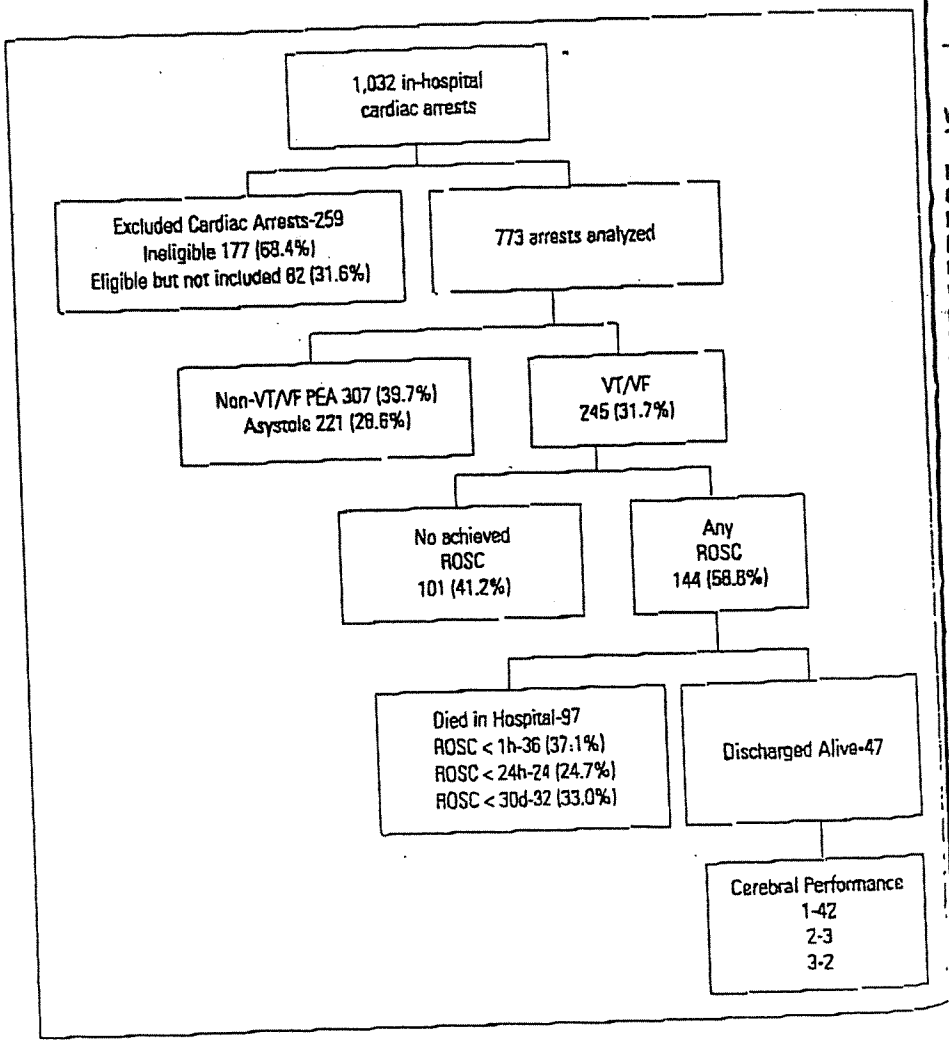

Figure 1.
Course of patients undergoing cardiac arrest during study. Eligibility criteria for study are listed in the Methods section. Cerebral performance refers to patients' cognitive function classification at hospital discharge. A rating of 1 indicates good function; 2 indicates moderate cerebral disability; and 3 indicates severe cerebral disability.[51] *VT/VF, Ventricular tachycardia or fibrillation; ROSC, return of spontaneous circulation.*

time from the start of CPR to defibrillation was significantly shorter in a successful resuscitation (4.9 minutes versus 8.0 minutes; $P<.001$). Survivors were more likely to have ventricular tachycardia or fibrillation (VT/VF) as their initial cardiac rhythm (40.6% versus 27.2%; $P<.001$) and were more likely to have a respiratory problem initiating their arrest (26.0% versus 11.6%; $P<.001$). Chronic ischemic heart disease was less prevalent in survivors (44.6% versus 51.0%; $P=.09$), but they were more likely to have a chronic respiratory disease (19.0% versus 13.7%; $P=.05$).

Table 2 displays the association of cardiac drug use and resuscitation outcome. Patients whose resuscitation was unsuccessful were significantly more likely to have received each of the ACLS medications except for bretylium. None of the drugs was significantly associated with an improved resuscitation outcome. Calcium was the only drug for which earlier administration was significantly associated with survival (survivors 8.47 minutes versus nonsurvivors 15.00 minutes; $P<.001$).

Using multivariate logistic regression, the association between each drug with resuscitation outcome was determined while controlling for confounding patient (age, gender, and previous cardiac or respiratory disease) and arrest (initial cardiac rhythm and cause) variables (Table 3). Odds ratios less than 0 indicate that drug administration was associated with a worse resuscitation outcome. The administration of almost all medications was significantly associated with a worse outcome. For each model, the likelihood ratio test was significant ($P<.001$) indicating that, overall, the model fit the data well. For all drugs, the models fit the data well as indicated by Hosmer-Lemeshow statistics that were greater than .2. Exceptions to this included calcium ($P=.08$) and bretylium ($P=.18$), whose models did not fit the data well. For each model, fewer than 10 observations (1.2%) had studentized residuals of more than 2.0.

To determine whether the association between cardiac drug use and resuscitation outcome varied with the initial cardiac rhythm, separate logistic regression models were performed for patients whose initial cardiac rhythm was VF/VT, pulseless electrical activity (PEA), or asystole (Table 4). Again, these models controlled for the effect of all significant confounding variables. Even when stratified by initial cardiac rhythm, none of the cardiac medications was associated with an improved outcome. Epinephrine, atropine, and bicarbonate were significantly associated with death in all 3 rhythm groups. The only medication whose association with resuscitation outcome varied significantly with initial cardiac rhythm was atropine, with slightly better outcomes when the initial rhythm was PEA. For patients whose initial cardiac rhythm was ventricular tachycardia or fibrillation, the inclusion of "time to defibrillation" in

Table 3.
Multivariate association between cardiac drugs and resuscitation outcome.

Drug	No. Patients Receiving Drug	Odds Ratio	95% Confidence Interval
Epinephrine	683	.08	.04, .14
Atropine	579	.24	.17, .35
Bicarbonate	257	.31	.21, .44
Calcium	105	.32	.18, .55
Lidocaine	214	.48	.33, .71
Bretylium	53	.55	.29, 1.07

The dependent variable is survival to 1 hour. An odds ratio less than 1.0 indicates the variable is associated with a decreased probability of survival at 1 hour. The effects of patient age and gender, initial cardiac rhythm, suspected cause of arrest, and chronic cardiac or respiratory disease were controlled for in all models

Table 4.
Association between cardiac drugs and resuscitation outcome based on initial cardiac rhythm.

Variable	No. Receiving Drug	Odds Ratio	95% Confidence Interval
Initial rhythm ventricular tachycardia or fibrillation (n=245)			
Epinephrine	199	.06	.02, .15
Atropine	160	.16	.09, .29
Bicarbonate	75	.41	.23, .74
Calcium	32	.32	.13, .79
Lidocaine	42	.53	.31, .90
Bretylium	36	.56	.26, 1.23
Initial rhythm pulseless electrical activity (n=307)			
Epinephrine	267	.09	.04, .25
Atropine	221	.39	.21, .70
Bicarbonate	111	.25	.13, .48
Calcium	37	.24	.08, .76
Lidocaine	48	31	.12, .78
Bretylium	10	.53	.09, 3.06
Initial rhythm asystole (n=221)			
Epinephrine	208	.11	.03, .43
Atropine	188	.23	.10, .51
Bicarbonate	67	.29	.14, .61
Calcium	35	41	.16, 1.05
Lidocaine	43	.49	27, 1.11
Bretylium	7	.39	.05, 3.43

The dependent variable is survival to 1 hour. An odds ratio less than 1.0 indicates the variable is associated with a decreased probability of survival at 1 hour. The effects of patient age and gender, initial cardiac rhythm, suspected cause of arrest, and chronic cardiac or respiratory disease were controlled for in all estimates.

trolling for resuscitation delay, endobronchial intubation, and whether the arrest was witnessed, epinephrine remained a predictor of unsuccessful resuscitation (odds ratio .5; 95% confidence interval .25–1.0).[25] Roberts et al[13] studied 310 consecutive in-hospital arrests and demonstrated a significant association between epinephrine and mortality (P=.0003). No improvement in survival was noted when higher doses of epinephrine were used during resuscitation.[26,27] In a randomized trial, patients who received epinephrine between countershocks had significantly lower resuscitation rates compared with those who received no drug.[7] Beurel et al[28] demonstrated that the administration of epinephrine was an independent predictor of death after in-hospital resuscitation. Increased amounts of epinephrine during resuscitation were significantly associated with acute renal failure after arrest, which is a significant predictor of death.[29]

Several physiologic explanations have been suggested to explain epinephrine's lack of benefit and possible harm.[30-32] However, the association of epinephrine and unsuccessful resuscitation is confounded by the increased probability of epinephrine utilization when patients are not revived. Although multivariate statistical methods attempt to adjust for this, the extremely heterogeneous and complex nature of patients undergoing cardiac arrest makes this a difficult feat.

This problem also applies to the rest of the ACLS drugs. We believe that randomized clinical trials are the best method of determining if new therapies, such as vasopressin,[33] improve outcomes when compared with standard ACLS drugs currently in use. With large randomized trials, treatment groups are balanced for both known and unknown confounders. Also, prospective trials permit the collection of the precise clinical parameters in which the drugs were administered. This information could be used in multivariate analyses to control for extraneous factors and possibly identify subgroups who might benefit from drugs given during resuscitation.

The effect of atropine and bicarbonate on resuscitation rates has also been questioned. Small case series have shown that atropine is beneficial during cardiac arrest.[34] Larger studies have produced conflicting results with some showing a significant benefit from atropine[4] and others showing none.[5] Animal models have shown no difference in recovery rates from PEA with atropine versus placebo.[35] In addition to epinephrine, the use of atropine has been associated with a significantly increased mortality for both in-hospital[36] and out-of-hospital[37] cardiac arrests. Laboratory[32] and clinical[38] studies evaluating the use of sodium bicarbonate also have produced conflicting results. The strongest evidence that raises doubt regarding bicarbonate's efficacy comes from a double-blind, randomized controlled trial of 245 patients where bicarbonate compared with placebo did not improve resuscitation outcome.[39]

Several studies of calcium during resuscitation have been performed. Small studies have shown a direct correlation between duration of resuscitation, low serum ionized calcium levels, and mortality. These observations have increased hope that calcium would improve resuscitation rates.[40] One randomized, blinded study with 90 patients showed a strong trend (P=.07) toward improved resuscitation rates for patients whose initial rhythm was PEA who were randomly assigned to the calcium arm.[41]

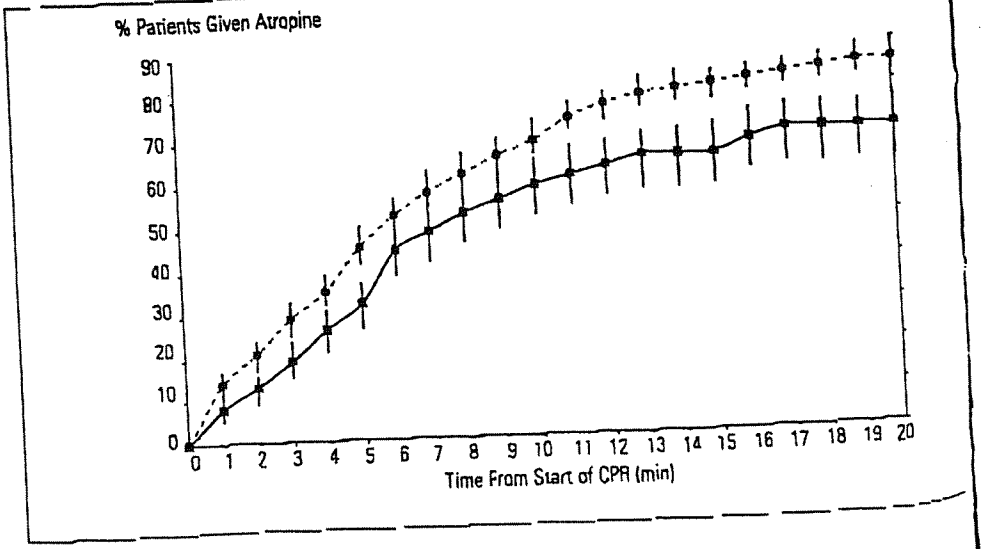

Figure 3.
Proportion of survivors and nonsurvivors receiving atropine. The figure shows the percentage of patients who received atropine by each minute of the resuscitation plotted for survivors (squares) and nonsurvivors (circles). These Cox proportional hazards models controlled for significant patient factors (including age, gender, and chronic history of cardiac or respiratory illness) and arrest factors (initial cardiac rhythm and cause of arrest). Ninety-five percent confidence intervals are provided.

tation. For example, 160 patients whose initial rhythm was ventricular tachycardia or fibrillation received atropine during the resuscitation (Table 4), indicating that in these patients asystole, PEA, or a slow pulseless rhythm likely developed at some time during the resuscitation.

Second, we did not determine whether the medications were administered by central or peripheral line, or whether peripheral administrations were followed by saline solution bolus and limb elevation.[45] Third, although all supervisors of the cardiac arrests had ACLS certification, we are unable to determine how compliant these physicians were with ACLS recommendations. Compliance with ACLS protocols, however, has not been shown to correlate with resuscitation outcome.[46,47] Fourth, although the logistic and Cox regression models fit our data well, we did not validate the models and are unsure if they would appropriately describe a different sample of cardiac arrests. In addition, our models did not explore interactions between the various ACLS medications and resuscitation outcome.

Finally, and most importantly, patients having cardiac arrest are extremely variable and complex. It may be naive to expect a significant benefit from a single medication in such a heterogeneous patient group. Many physicians recall cases where ACLS medication use seemed to be the difference between life and death for a particular patient. Perhaps a more accurate assessment of patient prognosis at resuscitation initiation[48] or invasive monitoring to guide therapy[49] would give these medications a better chance of showing a benefit. Further studies in this area must try to collect these and other important intra-arrest data to more accurately identify which patients benefit from these drugs.

In summary, our exploratory analysis of prospectively data collected data for 773 patients with in-hospital cardiac arrest associated the use of ACLS medications with increased mortality. We could not identify any subgroup of patients who may clearly benefit from any of these medications. Although further research into the treatment of patients not responding to defibrillation will be difficult,[50] it is necessary. We advocate the design and execution of large randomized clinical trials to determine whether other therapies improve resuscitation rates compared with the presently used ACLS drugs.

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Effect of Epinephrine and Lidocaine Therapy on Outcome After Cardiac Arrest Due to Ventricular Fibrillation

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One hundred ninety-nine patients with out-of-hospital cardiac arrest persisted in ventricular fibrillation after the first defibrillation attempt and were then randomly assigned to receive either epinephrine or lidocaine before the next two shocks. The resulting electrocardiographic rhythms and outcomes for each group of patients were compared for each group and also compared with results during the prior 2 years, a period when similar patients primarily received sodium bicarbonate as initial adjunctive therapy. Asystole occurred after defibrillation with threefold frequency after repeated injection of lidocaine (15 of 59, 25%) compared with patients treated with epinephrine (four of 55, 7%) ($p<0.02$). There was no difference in the proportion of patients resuscitated after treatment with either lidocaine or epinephrine (51 of 106, 48% vs. 50 of 93, 54%) and in the proportion surviving (18, 19% vs. 21, 20%), respectively. Resuscitation (64% vs. 50%, $p<0.005$) but not survival rates (24% vs. 20%) were higher during the prior 2-year period in which initial adjunctive drug treatment for persistent ventricular fibrillation primarily consisted of a continuous infusion of sodium bicarbonate. The negative effect of lidocaine or epinephrine treatment was explained in part by their influence on delaying subsequent defibrillation attempts. Survival rates were highest (30%) in a subset of patients who received no drug therapy between shocks. We conclude that currently recommended doses of epinephrine and lidocaine are not useful for improving outcome in patients who persist in ventricular fibrillation. Lidocaine administration is commonly associated with asystole, and any possible attribute of initial adjunctive drug therapy is outweighed by its detrimental effect on delaying successive shocks for persistent ventricular fibrillation. (*Circulation* 1990;82:2027–2034)

The rationale for specific drugs administered during cardiac arrest is primarily based on observations made during experimental animal studies or from patients with ventricular arrhythmias complicating acute myocardial infarction. The American Heart Association Guidelines for Advanced Cardiac Life Support emphasize the use of both epinephrine and lidocaine for patients who persist in ventricular fibrillation after initial attempts at defibrillation.[1] During experimental cardiac arrest, epinephrine administration results in higher rates of resuscitation, seemingly by augmenting myocardial blood flow during chest compression.[2–8]. Lidocaine is also often used to treat persistent ventricular fibrillation because the drug has been shown in some studies to prevent the emergence of ventricular fibrillation during the early hours of acute myocardial infarction.[9–11] Other studies, however, have shown that lidocaine increases defibrillation energy level requirements and is relatively ineffective in terminating ventricular tachyarrhythmias after they have been established.[12–17]

Ventricular fibrillation persists after initial defibrillation attempts in 25–40% of patients discovered in cardiac arrest and may present a condition quite different from either acute myocardial infarction or experimental resuscitation, and thus may have different drug requirements.[18,19] The purpose of this trial was to determine prospectively whether the initial administration of either epinephrine or lidocaine improved resuscitation results in patients discovered in ventricular fibrillation that was refractory to an initial defibrillation attempt.

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Methods

The Seattle Emergency Medical System is a tiered response system. The first level of care is provided by firefighters. At the time of the study (mid-1980s), they, with rare exception, provided only cardiopulmonary resuscitation until paramedics arrived and took charge of the resuscitation effort. The second level of care is provided by paramedics, trained and equipped to provide endotracheal intubation, defibrillation, and intravenous drug therapy, practicing either under written standing orders or remote verbal prescription of a physician.

For several years before this study, the protocol for treatment of ventricular fibrillation was to deliver one countershock and then, if ventricular fibrillation persisted, place an endotracheal tube and intravenous catheter. A continuous infusion of sodium bicarbonate was administered and continued until further resuscitation efforts either resulted in an organized, perfusing rhythm or until 180 meq had been infused.

During this 2-year study ending in 1985, the treatment protocol was modified. Depending on the calendar day (odd number or even number), patients who persisted in ventricular fibrillation after the first 200-J shock were assigned to receive either a 100-mg bolus of lidocaine or a 0.5-mg bolus of epinephrine (open label) through a peripheral intravenous cannula before a second 200-J shock was given. If ventricular fibrillation persisted after the second shock, a second bolus of the assigned drug was authorized and was followed by a third 360-J shock. After this point, additional epinephrine or lidocaine (for those patients who had not previously received lidocaine) was authorized. The resuscitation attempt was continued until the patient either regained an organized rhythm or became refractory to all treatment and was declared dead.

During this 24-month study, a total of 471 patients were discovered in cardiac arrest and ventricular fibrillation by paramedics. Ninety-eight were excluded from the trial because each had received either intravenous drug therapy or defibrillation attempts given by specially staffed first-response units before paramedic arrival (advent of enhanced first-level services). Thus, 373 patients with cardiac arrest due to ventricular fibrillation were potential candidates for the lidocaine/epinephrine drug comparison.

The paramedics' defibrillator monitors (Lifepak 5, Physio-Control Corporation, Redmond, Washington) were modified so that electrocardiographic (ECG) rhythm would be continuously recorded on magnetic tape. These tape recordings were reviewed to determine the times of drug administration and rhythms before and after each defibrillation attempt. Unfortunately, the miniature magnetic tape recording systems for this purpose are relatively unreliable (tape drive, cassettes, and limited battery capacity), and nearly one fourth of the resuscitations were not recorded. The rhythms were grouped as follows: ventricular fibrillation, asystole, supraventricular rhythms, and idioventricular rhythms (QRS complexes>110 msec and no discernible atrial activity). The patients' prehospital and hospital records were reviewed to determine clinical and demographic factors, emergency response times, and hospital outcome for each patient.

To put the findings from this 2-year trial in overall perspective, we compared results with those in similar patients treated during the prior 24 months. In this control period, 630 comparable patients were discovered in ventricular fibrillation by Seattle Fire Department paramedics. Again, excluding those given drug therapy or early defibrillation by first responders before paramedic arrival, 500 (79%) patients provided a group for historical comparison. The protocol for resuscitation during this earlier 2-year period was the same as during the drug study, with the exception of the type of initial drug therapy prescribed. A continuous infusion of sodium bicarbonate was most often the only drug administered between the first two shocks. Treatment with epinephrine or lidocaine between shocks 1 and 2 was unusual.

Discrete variables were compared among patients in the lidocaine, epinephrine, and historical control groups by using χ^2 analysis or Fisher's exact test. Continuous variables were compared between treatment groups by using Student's t test or analysis of variance. Multivariate analyses (logistic regression) were used to determine the effects of drug treatment and outcome. Where appropriate, the results were analyzed on the basis of intention to treat and actual treatment received.

Results

Patient Characteristics

During the 2-year period of epinephrine and lidocaine administration for treatment of persistent ventricular fibrillation, 373 patients were discovered by paramedics to be in cardiac arrest due to ventricular fibrillation; 199 (53%) persisted in ventricular fibrillation after the first 200-J shock. By odd/even calendar day, 106 of the 199 patients were allocated to receive lidocaine after shock 1, and 93 were allocated to epinephrine treatment. Of the total 199 patients with persistent ventricular fibrillation in both groups, 147 (74%) had adequate tape recordings for analysis of the ECG rhythm before and after shock 2; for the remainder, the recorder malfunctioned (battery or tape-drive problems) and no tape was available. The amplitude of ventricular fibrillation was greater than 200 μV in 129 (88%) and lower than 200 μV in 18 (12%) of the 147 patients in whom the resuscitation was recorded on tape.

Drug Assignment

Seventy (66%) of the 106 patients allocated to receive lidocaine received a bolus, per protocol, after shock 1. Thirty-four (49%) of the 70 patients treated

TABLE 1. Comparison of Clinical and Emergency System Characteristics of Patients Assigned to Lidocaine and Epinephrine for Persistent Ventricular Fibrillation After Shock 1*

Characteristics	Lidocaine (n=106)	Epinephrine (n=93)	Sodium bicarbonate (n=224)
Age (yr±SD)	67.5±13.2	66.3±1.3	65.6±12.6
Emergency dispatch to first response arrival (min±SD)	3.5±1.3†	3.1±1.4†	3.1±1.4
Emergency dispatch to paramedic arrival (min±SD)	6.9±3.4	6.3±2.7	6.8±3.2
Emergency dispatch to first shock (min±SD)	9.7±4.0	9.2±4.8	9.3±3.2
Male sex (%)	89 (84)	77 (83)	177 (79)
Witnessed collapse (%)‡	76 (72)	72 (77)	168 (77)
Bystander-initiated CPR (%)	34 (32)†	47 (50)†	73 (33)

*Findings in a comparable historical control group from the prior 2 years are also shown. During that time, sodium bicarbonate was the predominant drug infused between shocks 1 and 2. CPR, cardiopulmonary resuscitation.
† $p<0.05$ between the patients in the lidocaine and epinephrine groups.
‡ Percentages are adjusted for known cases.

with lidocaine failed to defibrillate after a second 200-J shock; 29 of these 34 patients then received a second bolus of lidocaine and a third shock was given. Of the remaining five patients, one received both lidocaine and epinephrine and four received no drug between shocks 2 and 3.

Thirty-six (34%) of the 106 patients initially allocated to lidocaine treatment received either a sodium bicarbonate infusion alone (n=13) or no drug before shock 2 (n=15). A few others inadvertently received either epinephrine (n=6) or both study drugs (n=2). Seventeen patients in this subset of 36 failed to defibrillate after shock 2; 11 received a bolus of lidocaine (late treatment) before shock 3. Thus, in all, 83 (78%) of the 106 patients allocated to lidocaine received one or more boluses of lidocaine before shock 3 for treatment of persistent ventricular fibrillation; 53 patients (50%) received 100 mg, and 30 (28%) received 200 mg.

For the 93 patients allocated to receive epinephrine, 58 (62%) received a 0.5-mg bolus after shock 1. Thirty (32%) of these failed to defibrillate with the second shock; 27 of the 30 received a second bolus before a third defibrillation attempt. For the three remaining patients, one received sodium bicarbonate and two received no drug before shock 3.

Inadvertently, 35 (38%) of the 93 patients initially assigned to epinephrine treatment received either sodium bicarbonate alone (n=17), no drug (n=15), or lidocaine (n=3) before shock 2. Of the 24 patients in this subset who failed to defibrillate with the second shock, 15 received epinephrine before shock 3 (late treatment). In all, 70 (75%) of the 93 patients allocated to receive epinephrine for persistent ventricular fibrillation received one or more injections before the third shock, including 43 (46%) who received one injection and 27 (29%) who received two.

Considering the *actual treatment received* by patients with ventricular fibrillation persisting after either the first or second shocks, 86 (43%) were treated with lidocaine, 79 (40%) received epinephrine, five (2%) received both drugs, 15 (8%) received no drug treatment, and 14 (7%) received simply a continuous infusion of sodium bicarbonate during this initial phase of the resuscitation attempt.

Table 1 compares the age and emergency vehicle response times (surrogate measures of the delay from collapse to initiation of cardiopulmonary resuscitation and defibrillation) for the patients in the two drug treatment groups. The response times were similar for patients who received epinephrine treatment and patients who received lidocaine treatment. By chance, a greater proportion of the patients in the epinephrine group received cardiopulmonary resuscitation initiated by a bystander (46% vs. 29%, respectively; $p<0.02$). From the taped recordings, the time of the first shock was 9 minutes after the emergency call. Approximately 4 minutes were required for intubation and intravenous cannulation after shock 1. The second shock was delivered an average of 14±4 minutes after the emergency call for patients in both treatment groups.

ECG Findings After Treatment and Shocks 2 and 3

There were no significant differences in the resulting rhythms between the patients in the two treatment allocation groups after shock 2 (Table 2). One hundred thirty-nine (70%) of the 199 patients with cardiac arrest had taped resuscitations in which the rhythm was recorded from the time of attachment of the electrodes until cardioversion. The proportion of patients with each rhythm at the end of the protocol was as follows: supraventricular rhythm in 31 (22%), ventricular fibrillation in 44 (32%), idioventricular in 43 (31%), and asystole in 21 (15%). Approximately 20% of patients in both treatment allocation groups developed a supraventricular rhythm after the second shock. There was, however, a trend after both shock 2 and 3 toward an increased incidence of asystole in patients who were randomized to receive lidocaine and a lesser trend toward more persistent ventricular fibrillation in those who received epinephrine.

Because some patients received the allocated drug late in the protocol (after the second shock) and there was a small proportion of crossover between groups, the resulting rhythm was analyzed

TABLE 2. Rhythm After Shock 2, Shock 3, and at End of Treatment Protocol by Intention-to-Treat Patients Given Either Lidocaine or Epinephrine for Persistent Ventricular Fibrillation, and a Subsequent Shock Was Delivered

	Lidocaine group			Epinephrine Group		
Rhythm	After shock 2 *n* (%)	After shock 3 *n* (%)	End of protocol *n* (%)	After shock 2 *n* (%)	After shock 3 *n* (%)	End of protocol *n* (%)
Supraventricular	14 (19)	2 (6)	16 (22)	12 (18)	3 (8)	15 (23)
Ventricular fibrillation	33 (44)	19 (59)	19 (26)	39 (59)	25 (66)	25 (38)
Idioventricular	19 (25)	4 (12)	23 (31)	11 (17)	9 (24)	20 (31)
Asystole	9 (12)	7 (22)	16 (22)	4 (6)	1 (3)	5 (8)

Tape recordings of the resuscitation and rhythms were available in 141 of 199 patients who persisted in ventricular fibrillation after shock 1 and in 70 of 105 patients who persisted in ventricular fibrillation after shock 2.

according to actual treatment received. Eighty-six patients received at least one bolus of lidocaine before the third shock and 79 received epinephrine before the third shock. Taped resuscitations were available in 59 (69%) of the patients treated with lidocaine and 55 (70%) of the patients treated with epinephrine. Asystole followed defibrillation threefold as frequently after treatment with lidocaine than with epinephrine, that is, 15 of 59 (25%) versus four of 55 (7%) ($p<0.02$) (Figure 1). The proportion of patients persisting in ventricular fibrillation at the end of the protocol was similar for both those receiving lidocaine and those receiving epinephrine, that is, 20 of 59 (34%) and 21 of 55 (38%), respectively. The proportion of patients treated with lidocaine who converted to a supraventricular rhythm, however, was half that observed in those who received epinephrine, or seven of 59 (12%) versus 13 of 55 (24%). Thus, the distribution of resulting rhythms (supraventricular, ventricular fibrillation, idioventricular, and asystole) was significantly different for the patients receiving the two treatments ($p<0.05$; test for trend, $p=0.01$), when the resulting rhythms were ordered and analyzed per drug given. This particular order was chosen because it is related to a descending likelihood of survival.[18]

The total number of shocks delivered during resuscitation was greater for patients allocated to epinephrine than for those patients assigned to lidocaine (6.4±4.2 vs. 5.2±3.9, respectively; $p=0.03$), reflecting the association of persistent ventricular fibrillation with epinephrine treatment and asystole with lidocaine treatment.

Patient Outcome for the Two Treatments

Approximately one half of the patients were resuscitated and admitted to the hospital (Figure 2). The proportion of patients either fully awake or partially responsive at the time of admission (a finding consistent with rapid resuscitation) was similar for both treatment groups, that is, nine of 48 (19%) and seven of 46 (15%), respectively. Hospital mortality rates after admission were also comparable; 30 (59%) of the 51 patients assigned to lidocaine and 32 (64%) of the 50 patients assigned to epinephrine died after admission. Overall, 21 (20%) of the 106 patients assigned to lidocaine and 18 (19%) of the 93 patients in the epinephrine group were discharged from the hospital.

Outcomes were also similar when analyzed by drug treatment received. Thirty-six (42%) of the 86 patients treated with lidocaine and 40 (51%) of the 79 patients treated with epinephrine were admitted to

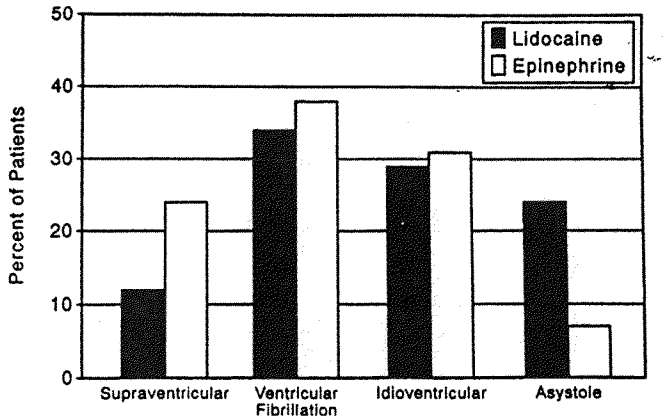

FIGURE 1. *Bar graph of rhythm results analyzed by actual treatment received. Asystole was threefold as frequent after initial use of lidocaine than after epinephrine ($p<0.02$). Taped rhythms were available in 70% of patients in both drug groups. Rhythms tabulated are those either after shock 3 for persistent fibrillation or after the first conversion before that time.*

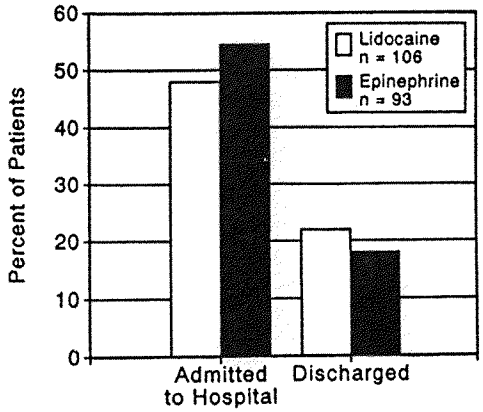

FIGURE 2. *Bar graph of outcome of patients who persist in ventricular fibrillation after shock 1 and who were assigned to lidocaine or epinephrine treatment before additional defibrillation attempts. The proportion of patients admitted to the hospital and discharged was similar for patients in both the epinephrine and lidocaine treatment groups during the study period.*

the hospital. The rates for survival to hospital discharge were 13 of 86 (15%) versus 14 of 79 (18%), respectively.

The overall 16% survival rate (28 of 170) for patients who received either drug was significantly lower than the 38% survival rate (11 of 29) in the subset who either received no drugs ($n=15$) or simply a continuous infusion of sodium bicarbonate before the second shock ($n=14$) ($p=0.01$).

Survival (hospital discharge) was then analyzed by type of treatment given in a multivariate analysis that considered the previously stated clinical and emergency response factors. Longer times from the emergency dispatch to the arrival of the first emergency vehicle (odds, 0.25; 95% confidence interval [CI], 0.05–1.18; $p=0.06$), the time to first shock (odds, 0.57; 95% CI, 0.34–0.95; $p=0.006$), and treatment with lidocaine or epinephrine (odds, 0.24; 95% CI, 0.08–0.76; $p=0.02$) were each predictive of worsened survival.

Lidocaine and Epinephrine Treatment Results Versus Results in Historical Controls (Sodium Bicarbonate)

The outcome of patients treated with lidocaine and epinephrine was compared with the outcome in a similar group of consecutive patients treated during the prior 2 years. During that earlier time, 224 patients persisted in ventricular fibrillation after the first shock. Tape recordings were available in 149 (67%) of these 224 patients. The protocol for intubation and intravenous cannulation between shocks 1 and 2 was the same as during the epinephrine/lidocaine study years. The type of drug therapy delivered between the first two shocks could be ascertained in 214 of the 224 patients from review of the resuscitation tapes and prehospital medical records. Sodium bicarbonate was infused in 132 patients (62%), 33 (15%) received either lidocaine or epinephrine plus sodium bicarbonate, three received some other drug combination, and 43 (19%) received no drug between the first two shocks.

Patient age, the proportion of patients with witnessed collapse, as well as the response time of emergency vehicles were similar to those for the 199 patients treated with lidocaine or epinephrine with persistent ventricular fibrillation (Table 1). The overall proportion of patients who received bystander-initiated cardiopulmonary resuscitation tended to be higher during the later period than during the early period, that is, 41% versus 33%, which might bias toward higher survival rates for patients treated with epinephrine or lidocaine. The time delay between shocks 1 and 2 was significantly longer in patients treated with epinephrine and lidocaine (5.0±2.0 vs. 4.1±2.7 minutes, $p=0.004$). This probably reflects the additional time required to administer a bolus of these drugs compared with the continuous infusion of bicarbonate initiated at the time of intravenous cannulation in the earlier 2 years.

One hundred forty-four (64%) of the 224 historical control patients were resuscitated and admitted to the hospital compared with 101 (50%) of the 199 patients during the epinephrine/lidocaine period ($\chi^2=7.92$; df=1, $p<0.005$). The proportion of patients discharged, however, was similar for both periods, that is, 54 of 224 (24%) versus 39 of 199 (20%), respectively.

A stepwise logistic regression analysis of survival in all patients with persistent ventricular fibrillation after shock 1 who were treated during the 4-year period was performed. Survival was positively correlated with witnessed collapse, younger age, shorter paramedic response time, bystander-initiated cardiopulmonary resuscitation, and male sex (Table 3). Survival was adversely related to receipt of lidocaine, epinephrine, or both, before the second shock for persistent ventricular fibrillation.

Time Between Shocks and Survival

The possible relation between the adverse effect of treatment with epinephrine or lidocaine and the attendant delay in administering these treatments was then examined. The time between shocks 1 and 2 was known in a subset of 296 patients with taped resuscitation attempts, 147 patients from the epinephrine/lidocaine period and 149 from the earlier period. As a first step, the stepwise logistic regression shown in Table 3 was repeated. Paramedic unit response time was used as a surrogate measure of the time from the emergency call until the first defibrillation to provide known values in the greatest number of patients. Drug treatments were grouped as

TABLE 3. Predictors of Survival to Hospital Discharge in Consecutive Patients With Persistent Ventricular Fibrillation After Shock 1

Variable	Odds ratio	95% CI	χ^2	p
Witnessed collapse	2.4	1.24–4.80	9.07	0.003
Age*	0.87	0.79–0.96	6.34	0.012
Paramedic response time†	0.73	0.56–0.95	6.49	0.011
Bystander-initiated CPR	1.78	1.06–2.97	4.73	0.030
Administration of lidocaine before shock 2	0.42	0.22–0.82	4.85	0.028
Male sex	2.00	0.95–4.21	3.63	0.057
Administration of epinephrine before shock 2	0.56	0.28–1.10	3.02	0.082

CI, confidence interval; CPR, cardiopulmonary resuscitation.
* Evaluated in 5-year increments for odds ratio and confidence interval.
† Evaluated in 3-minute increments for odds ratio and confidence interval.

either 1) lidocaine, epinephrine, or both drugs versus 2) sodium bicarbonate or no drug administered.

Unlike the prior multivariate analyses, survival in the subset of patients with tapes of resuscitation (required to tabulate the time between shocks) is higher in the historical control versus the epinephrine/lidocaine periods and may possibly bias results. Survival was 29.5% for taped patients and 13% for untaped patients during the first 2 years. For the lidocaine/epinephrine years, no bias is apparent, that is, there was 19.7% survival in taped patients versus 19.2% in untaped patients, respectively.

Although our ability to conclusively evaluate the effect of drug treatment versus time to shock is possibly hampered by this problem, the stepwise logistic regression analysis was repeated with the significant predictors of patient outcome in the model at the outset (witnessed collapse, age, paramedic response time, and bystander-initiated cardiopulmonary resuscitation). Drug treatment and minutes between shock 1 and shock 2 were free to enter the analysis. Only the time delay between shocks (and not drug treatment) was a significant predictor of survival after adjustment for the previously noted covariates (odds ratio, 0.75; 95% CI, 0.57–0.97), thus suggesting that the major negative effect of drug treatment was the time required to give it.

Figure 3 shows the admission and discharge rates for 411 patients with persistent ventricular fibrillation (all patients, taped and not taped, in whom drug treatment could be determined) after shock 1 and treatment with either epinephrine or lidocaine (176), a simple continuous infusion of sodium bicarbonate (162), or no drug treatment (73). Both hospital admission and discharge rates differed by treatment delivered, being lowest in those patients who received either epinephrine or lidocaine and highest in those receiving no drug treatment between shocks.

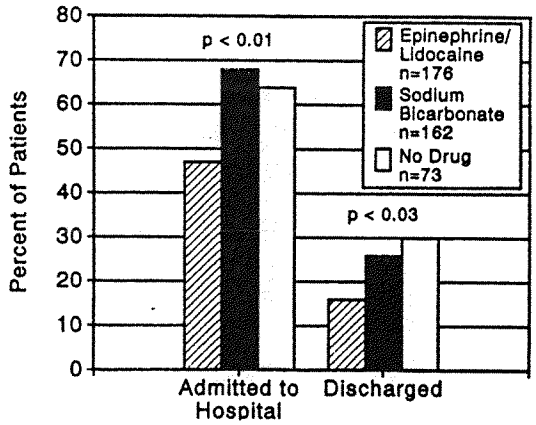

FIGURE 3. *Bar graph showing hospital admission and discharge rates in patients who persisted in ventricular fibrillation after the first defibrillation attempt. The results are based on findings over a 4-year period and include all patients who persisted in ventricular fibrillation and the treatment received, that is, epinephrine or lidocaine, sodium bicarbonate, or no drug treatment before the second shock. Hospital discharge rates were highest when no drug was administered for persistent fibrillation and repetitive shocks were instead delivered.*

Discussion

Two possible methods for improving outcome from cardiac arrest are to shorten the time to defibrillation as much as possible and to use a drug that can restore pulse and blood pressure when simple defibrillation does not. Rapid delivery of shocks to patients discovered in ventricular fibrillation is a significant predictor of successful outcome.[19–21] In contrast, most patients are not defibrillated immediately, and adjunctive pharmacological treatments are commonly used.

Clinical studies of drug treatment and their influence on resuscitation outcome after cardiac arrest are complicated to conduct and interpret. First, patients discovered in out-of-hospital cardiac arrest rarely respond immediately to pharmacological treatment. The circulation and distribution of the drug during chest compression is altered, and thus, the onset of effect is delayed. Interpretation of the results is further complicated by the fact that if one drug fails to elicit a prompt response during the protocol, the clinician will often use any other drug available to resuscitate the victim although the full effects of the first drug may not yet be evident. Epinephrine is currently recommended as adjunctive treatment in resuscitation despite the fact that the drug may precipitate arrhythmias and increase myocardial metabolic demands. One recent trial showed epinephrine superior to methoxamine during resuscitation, suggesting that the choice of initial drug therapy can make a difference.[22] An alternative approach for managing persistent ventricular fibrillation is to use an effective antiarrhythmic drug. One prior study failed to detect any benefit of lidocaine during resuscitation.[23]

The current study was a prospective evaluation of the initial use of lidocaine or epinephrine for patients who persisted in ventricular fibrillation after the first 200-J defibrillation attempt. Parenthetically, an earlier study had shown that both 200-J and 360-J energy level shocks were equally effective for the first two defibrillation attempts.[18] The purpose of this drug comparison was to determine which drug would prove more useful to treat persistent ventricular fibrillation, an antiarrhythmic drug or a drug aimed at augmenting perfusion during artificial circulation.

The interpretation of these results is complicated by the difficulty experienced by paramedics in adhering to a strict protocol during the highly charged and energetic effort of out-of-hospital resuscitation. When the first shock failed to cause defibrillation, only two thirds of the patients in each drug assignment group with persistent ventricular fibrillation initially received the assigned drug before the second shock, and three fourths of patients allocated to both lidocaine and epinephrine received the assigned drug before delivery of shock 3. On other occasions, shocks were delivered without intervening drug therapy, particularly if intravenous cannulation could not

be rapidly accomplished. In the tape recordings of resulting rhythms, there were trends but no significant differences between the two drug treatments (intention-to-treat analysis). Results based on actual treatment received showed otherwise. The use of lidocaine was associated with a threefold higher occurrence of asystole in subsequent defibrillation attempts. Lidocaine treatment of ambient ventricular ectopy has also been reported to cause asystole.[24,25]

The use of lidocaine, epinephrine, or both, between the initial two defibrillatory shocks was associated with poorer survival than in other patients with persistent ventricular fibrillation who received either only sodium bicarbonate or, instead, no drug treatment between shocks. Although the lack of tapes prevented an estimate of time between shocks in all cases, the adverse effect of epinephrine and lidocaine treatment for persistent fibrillation appeared related, at least in part, to the added time required to administer these drugs.

These results should not be interpreted to show that sodium bicarbonate, a drug with potentially adverse effects on cardiac resuscitation and hemodynamics, should be recommended for persistent ventricular fibrillation.[26–29] It was the practice in the Seattle paramedic system during the early 1980s to start a continuous infusion of sodium bicarbonate in patients who remained pulseless after initial defibrillation attempts. The rate of infusion was slow so that several minutes were required to infuse no more than 180 meq to those patients who did not reestablish a pulse after initial countershocks. In contrast, these results failed to uncover any adverse effect of sodium bicarbonate use during resuscitation. The dosage of epinephrine used also may be criticized as being insufficient to maximize hemodynamic effects; that is, a dose several-fold higher may be required and could have yielded quite different results. There are several experimental studies and case reports purporting a benefit with higher than standardly recommended doses of epinephrine.[30–35] This study, in fact, suggests that the current dose of 0.5–1.0 mg is ineffective, and the time required to give it is possibly detrimental. The clinical benefit and safety of higher epinephrine dosages is at present unclear, and the observations to date are inconsistent, some suggesting beneficial and others suggesting adverse effects with higher dosages.[34,36]

The difficulties encountered in this study highlight the obstacles in performing studies during resuscitation. The management of out-of-hospital cardiac arrest requires intense effort with limited personnel. Unless there is a major and immediate salutary effect associated with a treatment, its benefit may go undetected. In spite of these obstacles, the importance of such investigation is obvious and the prehospital setting provides a less complicated clinical situation than the hospital, where cardiac arrest is often the end result of complex metabolic disorders.

The findings here provide a rationale for rapid repeated shocks for the patient who initially fails defibrillation. This is consistent with another report that showed the superiority of defibrillation compared with initial drug treatment for the initial management of cardiac arrest.[37] It is unclear how many shocks should be repeated before drug therapy is initiated. Currently, three are recommended. The chance of defibrillation appears to be 50–60% with each attempt and is not influenced substantially by a prior failure. Perhaps, until an adjunctive pharmacological treatment is shown beneficial, even a greater number of shocks should be given, virtually assuring defibrillation (at least transiently) in all patients. The clinical importance of such an approach (lives saved), however, has yet to be shown.

Summary

In this study, there was no clinical evidence to support any form of drug therapy for initial treatment of persistent ventricular fibrillation. Drug treatment should be withheld until several repeated shocks have failed to restore an organized perfusing rhythm. The early use of lidocaine appears to cause asystole after countershocks. The present guidelines of three shocks for persistent ventricular fibrillation and then application of drug therapy need to be reexamined. Five successive shocks would achieve at least transient defibrillation in virtually all patients.

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KEY WORDS • lidocaine • epinephrine • ventricular fibrillation

Multicenter randomized trial and a systematic overview of lidocaine in acute myocardial infarction

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Background More than 20 randomized trials and 4 meta-analyses have been conducted on the use of prophylactic lidocaine in acute myocardial infarction (MI). The results suggest that lidocaine reduces ventricular fibrillation (VF) but increases mortality rates in acute MI.

Methods and Results Patients with ST-elevation MI who were examined <6 hours after symptom onset (n = 903) were randomly assigned to either lidocaine or no lidocaine and to either streptokinase and heparin or heparin alone. Lidocaine was given as 4 boluses of 50 mg each every 2 minutes, then an infusion of 3 mg/min for 12 hours, then 2 mg/min for 36 hours. We compared the incidence of in-hospital death and ventricular arrhythmias. We then performed a meta-analysis of prophylactic lidocaine in acute MI that included these and prior trial results. The rates of VF and death with and without lidocaine were calculated for each trial, then odds ratios (OR) with confidence intervals (CI) were calculated for the risk of these events overall with and without lidocaine. Patients given lidocaine in the randomized study had significantly less VF (2.0% vs 5.7% without lidocaine, $P = .004$) and a trend toward increased mortality rates (9.7% vs 7.0%, $P = .145$). Meta-analysis revealed nonsignificant trends toward reduced VF (OR 0.71, 95% CI 0.47 to 1.09) and increased mortality rates (OR 1.12, 95% CI 0.91 to 1.36) with lidocaine.

Conclusions Lidocaine reduces VF but may adversely affect mortality rates. The routine use of prophylactic lidocaine in acute MI is not recommended. (Am Heart J 1999;137:792-8.)

See related Editorial on page 770.

Despite significant advances over the last decade, high rates for early death persist after acute myocardial infarction (MI). Much of this early death results from ventricular fibrillation (VF), which typically occurs early after the onset of symptoms. Since the first use of lidocaine during the 1960s to prevent ventricular fibrillation (VF) with acute MI,[1] more than 20 randomized trials and 4 meta-analyses have studied its use.[2-5] There is now a general consensus that lidocaine prevents VF but at the expense of a possible increase in mortality, presumably because of bradyarrhythmias and asystole.[6]

The benefit or harm of the use of lidocaine in acute MI remains controversial. Previous trials have been limited by small sample sizes, short follow-up, inclusion of patients without confirmed MI, and nonstandard lidocaine regimens. In addition, most of these trials were conducted before the widespread use of thrombolytic therapy and may be less relevant to current clinical practice.

We performed a randomized trial of prophylactic lidocaine and streptokinase in patients with acute MI in Poland between 1986 and 1987. It is the largest single study of the use of intravenous lidocaine in acute MI in the thrombolytic era. In addition to reporting these results, we report an overview of the world's cumulative experience with the use of prophylactic lidocaine in acute MI.

Methods

Study population

Patients were considered for enrollment if they had chest pain lasting >30 minutes; had ST-segment elevation of ≥0.15 mV in ≥2 contiguous precordial leads or ≥0.1 mV in ≥2 limb leads; had no contraindication to intravenous lidocaine or nitroglycerin; and were examined at the hospital within 6 hours of symptom onset. Exclusion criteria included age >70 years, second- or third-degree atrioventricular block, severe sinus node dysfunction (heart rate <50 beats/min or sinus arrest >2 seconds), recent or current bleeding, known hemostatic disorders, history of cerebrovascular accident, surgical procedure within 1 month, uncontrolled hypertension (blood pressure >200/100 mm Hg), hypotension (systolic pressure <90 mm Hg) or shock, severe renal or hepatic dysfunction, gastrointestinal ulcer within the past 2 years, recent cardiopulmonary resuscitation, pregnancy, or any life-threatening condition.

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Table I. Baseline characteristics by lidocaine and streptokinase + heparin treatment groups

	Streptokinase + heparin		Heparin	
	Lidocaine (n = 178)	No lidocaine (n = 175)	Lidocaine (n = 170)	No lidocaine (n = 180)
Age (y)	54.4	52.6	53.9	53.8
Male	146 (82.0%)	143 (81.7%)	141 (82.9%)	143 (79.4%)
Height (cm)	169.6	170.1	169.6	169.0
Weight (kg)	76.0	76.2	73.8	77.2
Current smoking	113 (63.5%)	127 (72.6%)	120 (70.6%)	99 (55.0%)
Diabetes	19 (10.7%)	13 (7.4%)	17 (10.0%)	21 (11.7%)
Previous MI	32 (18.0%)	27 (15.4%)	34 (20.0%)	36 (20.0%)
Anterior MI	77 (43.3%)	65 (37.1%)	68 (40.0%)	64 (35.6%)
Inferior MI	97 (54.5%)	106 (60.6%)	93 (54.7%)	113 (62.8%)
Heart rate (beats/min)	78.6	78.0	80.0	79.7
Systolic blood pressure (mm Hg)	130.5	131.1	129.1	135.0
Killip class				
I-II	172 (96.6%)	170 (97.1%)	161 (94.7%)	172 (95.6%)
III-IV	6 (3.4%)	5 (2.9%)	9 (5.3%)	8 (4.4%)
Time to treatment (hr)*	2.7	2.6	2.7	2.7
Confirmed MI	174 (97.8%)	171 (97.7%)	162 (95.3%)	177 (98.3%)
Q-wave MI	161 (90.4%)	159 (90.9%)	146 (85.9%)	164 (91.1%)
Non-Q-wave MI	13 (7.3%)	12 (6.9%)	16 (9.4%)	13 (7.2%)

Data are given as medians or as number (%) of patients.
*Time from symptom onset to beginning of lidocaine therapy.

Table II. Clinical end points by lidocaine and streptokinase + heparin treatment groups

	Streptokinase + heparin			Heparin		
	Lidocaine (n = 178)	No lidocaine (n = 175)	P value	Lidocaine (n = 170)	No lidocaine (n = 180)	P value
Ventricular tachycardia	3 (1.7%)	11 (6.3%)	.023	5 (2.9%)	4 (2.2%)	.745
Ventricular fibrillation	4 (2.2%)	13 (7.4%)	.020	1 (0.6%)	7 (3.9%)	.068
Asystole/sinus node dysfunction	39 (21.9%)	33 (18.9%)	.476	17 (10.0%)	21 (11.7%)	.616
Atrioventricular block	27 (15.2%)	18 (10.3%)	.168	5 (2.9%)	16 (8.9%)	.016
In-hospital mortality rate	16 (9.0%)	11 (6.3%)	.338	13 (7.6%)	12 (6.7%)	.722

Data are given as number (%) of patients.

Olkin.[28] This is a random-effects model that reduces to a fixed-effects model when studies are homogeneous. Risk differences between control and treatment arms were computed for the events of each trial and combined by using the same model.

Results

Randomized trial

A total of 903 patients were enrolled and randomly assigned to lidocaine or no lidocaine. Of these, 703 had no contraindications to streptokinase and were also randomly assigned to either streptokinase plus heparin or heparin alone. Baseline characteristics by treatment group are shown in Table I. Patients randomly assigned to lidocaine were similar to patients randomly assigned to no lidocaine in sex, smoking status, diabetes, previous MI, heart rate, systolic blood pressure, baseline Killip class, time to treatment, and incidence of Q-wave MI. Patients randomly assigned to lidocaine were significantly lighter and had significantly fewer inferior MIs; they also tended to be older (by 1.1 years) and have more confirmed MIs.

Clinical outcomes by treatment group are shown in Table II. There was a trend toward increased mortality rates in patients given lidocaine compared with patients not given lidocaine (9.7% vs 7.0%, $P = .145$). Patients who received lidocaine had a significant reduction in VF (2.0% vs 5.7%, $P = .004$) and a trend toward a reduction in ventricular tachycardia (2.2% vs 3.5%, $P = .261$) compared with those who did not receive lidocaine. Lower rates of VF with lidocaine were seen both in patients randomly assigned to streptokinase plus heparin and in patients randomly assigned to heparin alone. There was no difference in

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Table III. Randomized trials of use of prophylactic lidocaine in acute MI

Trial	Included in meta-analyses	Year	Route	Analysis method	Lidocaine		
					n	Mortality (n)	VF (n)
Kostuk and Beanlands[7]	4,5	1969	IV	AMI	34	0	0
Bennett et al[8]	3,4,5	1970	IV	AMI	249	25	16
Mogensen[9]	3	1970	IV	AMI	91	12	0
Baker et al[10]	4,5	1971	IV	AMI	21	5	0
Chopra et al[11]	3,4,5	1971	IV	ITT	39	7	3
Pitt et al[12]	3,4,5	1971	IV	AMI	108	9	1
Darby et al[13]	3,4,5	1972	IV	AMI	103	12	4
O'Brien et al[14]	3,4,5	1973	IV	ITT	154	11	7
Bleifeld et al[15]	3	1973	IV	ITT	41	2	0
Lie et al[16]	3,4,5	1974	IV	AMI	107	8	0
Valentine et al[17]	3,5	1974	IM	AMI	207	18	ND
Sandler et al[18]	4,5	1976	IM	AMI	91	0	0
Singh and Kocot[19]	4,5	1976	IM	ITT	27	0	0
Lie et al[20]	3,4,5	1978	IM	AMI	147	5	6
Wennerblom et al[21]	3,5	1982	IM	ITT	71	5	0
Dunn et al[22]	3,4,5	1985	IM	ITT	207	8	0
Koster and Dunning[23]	3,4,5	1985	IM	ITT	2987	19	8
Hargarten et al[24]	3,5	1986	IM	ITT	222	18	2
Wyse et al[25]	4,5	1988	IV	ITT	168	8	0
Hargarten et al[26]		1990	IV	ITT	704	57	4
Sadowski et al		1998	IV	ITT	445	43	9
Total					6223	272	60

Acute myocardial infarction (AMI) includes only patients with confirmed acute myocardial infarction.
Mortality, latest reported all-cause mortality rate; *n*, number of patients enrolled on intention-to-treat basis; *IV*, intravenous; *IM*, intramuscular; *ND*, no data available.

lidocaine was seen in all subgroups of patients, including patients given streptokinase with heparin, heparin alone, and neither streptokinase nor heparin. Because of the smaller sample sizes of these subgroups, many of these differences did not reach statistical significance.

At baseline, patients who received lidocaine had significantly fewer inferior MIs and tended to be older and to have more confirmed MIs than those who did not receive lidocaine. These differences in baseline characteristics may reflect a higher baseline risk of death for patients randomly assigned to lidocaine and may partially explain the increased mortality rates seen in the lidocaine-treated patients in this trial.

It has been hypothesized that lidocaine increases mortality rates through an increase in bradyarrhythmias and asystole.[1,6] There was no detectable increase in asystole, sinus node dysfunction, or atrioventricular block in patients who received lidocaine. In fact, the subgroup of patients who received both heparin and lidocaine had a significantly lower rate of atrioventricular block than those who received heparin alone. This finding in an unexpected subgroup, however, probably reflects the play of chance. Whether lidocaine produces a higher rate of bradyarrhythmias and asystole remains controversial. Whatever the mechanism, this trial is consistent with the possibility that lidocaine therapy is associated with worse outcomes.

More than 20 randomized trials of prophylactic lidocaine use in acute MI were conducted between 1969 and 1990 (Table III).[7-26] Although some trials showed a reduction in VF with prophylactic lidocaine,[2,4] none had sufficient statistical power to determine whether lidocaine improves survival in these patients. Three meta-analyses of prophylactic lidocaine concluded that although lidocaine reduces VF after acute MI, it increases short-term mortality rates,[3-5] particularly in patients with confirmed MI,[3] possibly through an increased incidence of bradyarrhythmias.[4]

Our systematic overview included all randomly assigned patients, based on the "intention-to-treat" principle, and reported total VF and the latest reported all-cause mortality rates. Although the beneficial effects of lidocaine on VF are likely to be recognized early, lidocaine may have benefits and/or risks that are not apparent until later follow-up. Most of the trials reported in-hospital rates of VF and mortality, and several reported even shorter follow-up periods.

When only the trials from the prior meta-analyses were considered, lidocaine therapy was associated with trends toward reduced VF and increased mortality rates. The addition of the study by Hargarten et al[26] and the current trial to the overview increased the magnitude

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Randomized, Double-Blind Comparison of Intravenous Amiodarone and Bretylium in the Treatment of Patients With Recurrent, Hemodynamically Destabilizing Ventricular Tachycardia or Fibrillation

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Background After several days of loading, oral amiodarone, a class III antiarrhythmic, is highly effective in controlling ventricular tachyarrhythmias; however, the delay in onset of activity is not acceptable in patients with immediately life-threatening arrhythmias. Therefore, an intravenous form of therapy is advantageous. This study was designed to compare the safety and efficacy of a high and a low dose of intravenous amiodarone with bretylium, the only approved class III antiarrhythmic agent.

Methods and Results A total of 302 patients with refractory, hemodynamically destabilizing ventricular tachycardia or ventricular fibrillation were enrolled in this double-blind trial at 82 medical centers in the United States. They were randomly assigned to therapy with intravenous bretylium (4.7 g) or intravenous amiodarone administered in a high dose (1.8 g) or a low dose (0.2 g). The primary analysis, arrhythmia event rate during the first 48 hours of therapy, showed comparable efficacy between the bretylium group and the high-dose (1000 mg/24 h) amiodarone group that was greater than that of the low-dose (125 mg/24 h) amiodarone group. Similar results were obtained in the secondary analyses of time to first event and the proportion of patients requiring supplemental infusions. Overall mortality in the 48-hour double-blind period was 13.6% and was not significantly different among the three treatment groups. Significantly more patients treated with bretylium had hypotension compared with the two amiodarone groups. More patients remained on the 1000-mg amiodarone regimen than on the other regimens.

Conclusions Bretylium and amiodarone appear to have comparable efficacies for the treatment of highly malignant ventricular arrhythmias. Bretylium use, however, may be limited by a high incidence of hypotension. (*Circulation*. 1995;92:3255-3263.)

Key Words • amiodarone • bretylium • ventricles • fibrillation • tachycardia

Amiodarone has become a common therapy for patients with a variety of cardiac arrhythmias.[1,2] The oral formulation has been marketed in the United States since 1986 and is indicated for the treatment of recurrent ventricular fibrillation (VF) and hemodynamically destabilizing ventricular tachycardia (VT) when other antiarrhythmic drugs are ineffective or cannot be tolerated.[3-5] Intravenous amiodarone has been available for clinical use internationally and as an investigational drug in the United States for several years.[6-9] Reports of its efficacy in patients with incessant and/or refractory ventricular arrhythmias have been widely published, with efficacy rates ranging from 50% to 75% in most series.[10-15] Although several clinical studies showed it to be effective, most of these were uncontrolled, unblinded, and nonrandomized.

See p 3154

The present study is the third in a series of multicenter controlled trials that represent the first attempts to investigate the safety and efficacy of intravenous amiodarone (Cordarone Intravenous, Wyeth-Ayerst Laboratories) in a scientifically valid format. Because the intended study population was so ill, we designed a study in which all patients would receive active therapy with the study drug or an approved comparator. The comparator bretylium is the only intravenous class III antiarrhythmic agent currently approved in the United States for the treatment of life-threatening VT/VF.[16-18]

Methods

The study was a randomized, double-blind, parallel, positive-controlled, multicenter, inpatient design. Eighty-two centers participated; each enrolled between 1 and 27 patients. Patients were eligible for inclusion if they had incessant (recurring immediately after termination) VT, VF, or at least 2 (mean, 4.93) episodes of hemodynamically destabilizing VT or VF in

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*See the appendix for a complete list of the investigators and their centers.

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TABLE 2. Characteristics of the Study Population

Variable	Treatment Group: Amiodarone 125 mg (n=94)	Amiodarone 1000 mg (n=105)	Bretylium (n=103)
Sex, % male	77	76	75
Age, y (mean±SD)	66±12	63±12	66±12
Primary diagnosis, %			
HDVT	71	64	71
VF	7	11	11
Incessant VT	21	25	18
History of MI, %	76	84	86
Acute MI, %	6	8	10
EF, % (mean±SD)	31±13	28±10	31±12
Average NYHA class	2.8	2.6	2.7

HDVT indicates hemodynamic destabilizing ventricular tachycardia; VF, ventricular fibrillation; MI, myocardial infarction; EF, ejection fraction; and NYHA, New York Heart Association. There were no significant differences among treatment groups in any variables.

Efficacy

For the primary specified end point, hemodynamically destabilizing VT/VF events per hour during the double-blind period, we analyzed the data using rank scores and summarized the data using medians. The median is a better way of summarizing these data than the mean because the former is less influenced by patients who might have had a very large or small number of events at any given time point. As shown in Table 4, there were no statistically significant differences in the overall event rate among the treatment groups (P=.237). However, there were significant differences among the groups at the 6-hour time point (P=.049), and the differences approached significance at the 12-hour time point (P=.091). An analysis of event rates during the initial hours of drug administration indicated that >80% of all events occurred in the first 12 hours (Fig 1). In addition, >50% of the bretylium-treated patients discontinued blinded therapy before hour 16 and crossed over to open-label amiodarone.

The results of the time to first hemodynamically destabilizing VT/VF event analysis are shown (Fig 2) as the cumulative percentage of patients who remained event-free at a given time. Most of the events in the study occurred in the first 12 hours, and there was a higher event rate for patients treated with the 125-mg/

TABLE 3. Concomitant Cardiovascular Medications During Double-Blind Therapy

Concomitant Medication	Treatment Group: Amiodarone 125 mg (n=94)	Amiodarone 1000 mg (n=105)	Bretylium (n=103)
ACE inhibitors	24 (26)	22 (21)	13 (13)
Other vasodilators	41 (44)	33 (31)	35 (34)
Antiarrhythmics	1 (1)	6 (6)	6 (6)
Ca^{2+} blocker	4 (4)	5 (5)	5 (5)
β-Blocker	10 (11)	10 (12)	7 (7)
Anticoagulant	33 (35)	41 (39)	31 (30)
Positive inotropes	43 (46)	45 (43)	49 (48)
Diuretics	51 (54)	47 (45)	48 (48)

ACE indicates angiotensin-converting enzyme. There were no significant differences among treatment groups in any variables. Values are n (%).

TABLE 4. Median HDVT/VF Event Rate During Double-Blind Therapy

Time Period	Treatment Group: Amiodarone 125 mg (n=94)	Amiodarone 1000 mg (n=105)	Bretylium (n=103)	P
Overall	1.88	0.48	0.96	.237
Hours 0 to 6	4.08	0.00	0.00	.049
Hours 0 to 12	1.92	0.00	1.92	.091

HDVT indicates hemodynamic destabilizing ventricular tachycardia; VF, ventricular fibrillation; and Overall, during entire double-blind period. The hour 0 to 6 and 0 to 12 values were for all patients, regardless of whether they completed the interval. Values are HDVT/VF events/24 h.

24-h dose of amiodarone. When this analysis was carried out for the first 12 hours, the log-rank test approached statistical significance (Fig 3). By hour 48, the differences among the three treatment groups were indistinguishable because more patients had received supplemental infusions of study drug or had discontinued double-blind treatment and crossed over to open-label amiodarone therapy. In fact, the protocol-specified high-to-low amiodarone dose ratio of 8:1 was compressed to a dose ratio of only 1.8:1.

Although this study was not designed to determine the effects of these agents on the termination of arrhythmia, the incessant-VT population provided an opportunity to examine these effects. In this study, incessant VT was defined as recurrent VT despite attempted cardioversion. Because of the small number of patients enrolled while having incessant VT (ie, incessant VT at the time of initiation of double-blind therapy), there was insufficient power to detect statistically significant differences among treatment groups. A log-rank test revealed an overall among-group value of P=.62. However, numerical differences among groups were seen in the median time from initiation of therapy to termination of incessant VT, as follows: bretylium, 6.98 hours (n=9); low-dose amiodarone, 4.58 hours (n=13); and high-dose amiodarone, 4.23 hours (n=12).

Table 5 illustrates the number of supplemental infusions administered to each group. The table summarizes the results by treatment group, the number of supplemental infusions administered during the double-blind phase of the study, and the number of supplemental

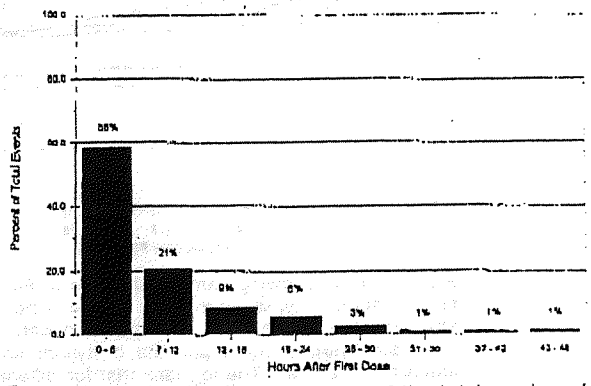

FIG 1. Bar graph showing percentage of the total number of arrhythmic events (hemodynamic destabilizing ventricular tachycardia or ventricular fibrillation) that occurred in each 6-hour interval during first 48 hours after study initiation.

TABLE 5. Number and Comparison of Supplemental Infusions During Double-Blind Period

Variable	Dose Group (n)				Paired P Values		
	Amio 125 mg (n=94)	Amio 1000 mg (n=105)	Bret (n=103)	P*	B vs L	B vs H	L vs H
Total Infusions							
Mean (SD)	2.11 (2.01)	1.58 (1.88)	1.21 (1.76)	.001	<.001	.073	.050
Median	1.00	1.00	0.00				
Supplemental Infusions per hour							
Mean (SD)	0.16 (0.26)	0.16 (0.36)	0.22 (0.50)	.323	...	...	...
Median	0.00	0.00	0.00				

Amio indicates amiodarone; bret, bretylium; B vs L, bretylium vs low-dose (125 mg) amiodarone; B vs H, bretylium vs high-dose (1000 mg) amiodarone; and L vs H, low-dose vs high-dose amiodarone.
* By Cochran-Mantel-Haenszel procedure.

dose amiodarone patients). Twenty-five patients died while receiving open-label amiodarone (13 bretylium patients, 7 high-dose amiodarone patients, and 5 low-dose amiodarone patients). We also counted the number of deaths that occurred after discontinuation of study drug, either blinded or open-label. Fifty-eight patients died while not receiving any drug, including 21 randomly assigned to the bretylium group and 20 and 17 randomly assigned to the 1000- and 125-mg amiodarone dose groups, respectively. These 58 patients included 25 patients who died after being assigned "do not resuscitate" status at the request of their families.

Fig 6 shows the cumulative number of patients in each treatment group who remained on double-blind therapy at each hour. This took into account treatment failures or adverse effects that might have prompted drug discontinuation. Overall, more patients withdrew from bretylium therapy than from amiodarone therapy ($P=.070$), with more bretylium patients discontinuing double-blind therapy in each category (treatment failures: bretylium, 22%; high-dose amiodarone, 19%; and low-dose amiodarone, 24%; adverse effects: bretylium, 10%; high-dose amiodarone, 6%; and low-dose amiodarone, <1%). During the first 6 and 12 hours, there were a significantly greater number of discontinuations from the bretylium dose group for both treatment failures and lack of efficacy than from the amiodarone dose groups ($P=.004$ and $P=.036$, respectively). For the remainder of the double-blind period, the curves paralleled each other, because the numbers of events in all groups were greatly reduced during the final 36 hours of the study.

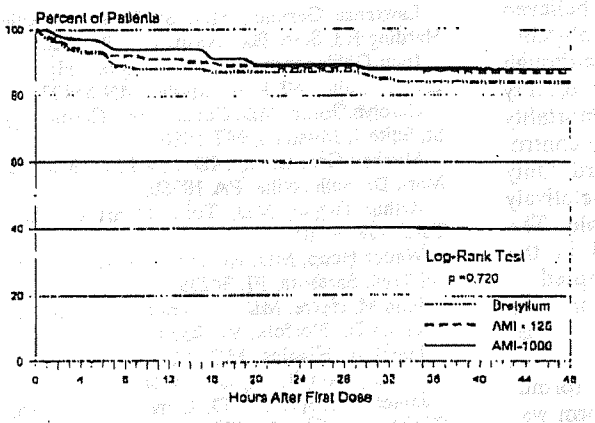

FIG 4. Graph showing cumulative percentage of patients who survived during the first 48 hours of the study. Mortality was low and not significantly different among the groups (log-rank test: $P=.7202$). AMI indicates amiodarone.

Discussion

The treatment of patients with life-threatening ventricular arrhythmias remains one of the most difficult challenges of contemporary medicine.[19,20] Particularly difficult are cases in which the arrhythmias recur frequently and cause hemodynamic instability. The mortality of such patients, despite aggressive therapy, has been reported to be >80% to 90% in small uncontrolled series.[21,22] Parenteral drugs currently available to treat such patients either are ineffective or cause potentially serious adverse effects, such as hypotension, heart block, torsade de pointes, cardiac arrest, and asystole, that contribute to hemodynamic deterioration.

Intravenous amiodarone is the newest agent to be used in this clinical situation. To date, the results of clinical trials have been quite encouraging, with reported response rates of 50% to 75% with a reasonable side-effect profile.[10-15] Most of the studies have been limited by the lack of a control group or randomization, or they used retrospective analyses. We believed that the target population was too sick to be enrolled in a placebo-controlled study, even though such a study would have been ideal to gain approval from regulatory agencies.

To demonstrate the efficacy of intravenous amiodarone, three multicenter trials enrolled ≈1000 patients with life-threatening VT/VF. The first trial was a dose-ranging study.[23] The second study, reported in this issue of *Circulation* (Scheinman et al), was also a dose-ranging study in which a broader dose range was examined. These studies were based on the principle that responses to different doses provide evidence of clinical effect. The second dose-ranging study demonstrated a difference in efficacy and tolerance among the three doses used. The study reported here was the third in the series. Two doses of intravenous amiodarone were compared with an approved drug, bretylium, recognized to be effective in patients with highly malignant arrhythmia. The high and low doses of amiodarone used in the second dose-ranging study were compared with the dose of bretylium recommended in its package insert. The patient population was quite ill, and thus, provisions were made for patients to receive only active therapy. Supplemental doses of study drug were permitted for breakthrough arrhythmias. In addition, investigators were permitted to switch to open-label intravenous amiodarone if supplemental doses of blinded study drug were not effective.

Recommended Policies/Procedures, Treatment Protocols, and Quality Assurance of the Procedure or Medication

PROCEDURE

CPR until defibrillator available then:
Defibrillate
200 J, 300 J 360 J
Oxygen
Intubate
IV LR

Epinephrine 1:10,000
1.0 mg IVP or 2.0 mg ET

If VT/VF continues:
Repeat q 3 minutes

**Defibrillate within 30 - 60 seconds of drug administration

****Amiodarone**
300 mg IVP
follow with 10cc
NS IV flush

VF/VT Continues?

Yes

** Lidocaine
Initial dose:
1 - 1.5 mg/kg IVP or
2-3 mg/kg ET
Consider repeat same
dose q 3-5 mins
Maximum dose:
3 mg/kg IV 6 mg/kg ET

No

Go to Policy:
#7204 **Asystole**
#7205 **PEA**
#7208 **Return of Spontaneous Circulation**

NOTES:

Amiodarone may not be administered by ETT

Administer amiodarone once only

MEDICAL CONTROL

Amiodarone will be administered under standing orders for pulseless retractory ventricular tachycardia/fibrillation only.

QUALITY "ASSURANCE"

Each case utilizing amiodarone will be individually tracked. Using the existing cardiac arrest survival database, rates will be calculated for cardiac arrest survival from ventricular fibrillation before and after the institution of amiodarone.

Description of the Training and Competency Testing

TRAINING MATERIALS
AMIODARONE HCl

MECHANISMS OF ACTION

Amiodarone is generally considered a class III antiarrhythmic drug, but it possesses electrophysiologic characteristics of all four Vaughan Williams classess. Like class I drugs, amiodarone blocks sodium channels at rapid pacing frequencies, and like class II drugs, it exerts a noncompetitive antisympathetic action. One of its main effects, with prolonged administration, is to lengthen the cardiac action potential, a class III effect. The negative chronotropic effect of amiodarone in nodal tissues is similar to the effect of class IV drugs. In addition to blocking sodium channels, amiodarone blocks myocardial potassium channels, which contributes to slowing of conduction and prolongation of refractoriness. The antisympathetic action and the block of calcium and potassium channels are responsible for the negative dromotropic effects on the sinus node and for the slowing of conduction and prolongation of refractoriness in the antrioventricular (AV) node. Its vasodilatory action can decrease cardiac workload and consequently myocardial oxygen consimption. Cordarone I.V. administration prolongs intranodal conduction (Atrial-His, AH) and refractoriness of the antrioventricular node (ERP AVN), but has little or no effect on sinus cycle length (SCL), refractoriness of the right atrium and right ventricle (ERP RA and ERP RV), repolarization (QTc), intraventricular conduction (QRS), and infranodal conduction (His-ventricular, HV).

INDICATIONS AND USAGE

Cordarone I.V. is indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy.

CONTRAINDICATIONS

Cordarone I.V. is contraindicated in patients with known hypersensitivity to any of the components of Cordarone I.V., or in patients with cardiogenic shock, marked sinus brachycardia, and second- or third-degree AV block unless a functioning pacemaker is available.

WARNINGS

Hypotension

Hypotension is the most common adverse effect seen with Cordarone I.V. in clinical trials, treatment-emergent, drug-related hypotension was reported as an adverse effect in 288 (16%) of 1836 patients treated with Cordarone I.V. Clinically significant hypotension during infusions was seen most often in the first several hours of treatment and was not close related, but appeared to be related to the rate of infusion. Hypotension necessitating alterations in Cordarone I.V. therapy was reported in 3% of patients, with permanent discontinuation required in less than 2% of patients. Hypotension should be treated initially by slowing the infusion; additional standard therapy may be needed, including the following: vasopressor drugs, positive inotropic agents, and volume expressions. ***The initial rate of infusion should be monitored closely and should not exceed that prescribed in DOSAGE AND ADMINISTRATION.***

Bradycardia and AV Block
Drug-related bradycardia occurred in 90 (4.9%) of 1836 patients in clinical trials while they were receiving Cordarone I.V. for life-threatening VT/VF; it was not dose-related. Bradycardia should be treated by slowing the infusion rate or discontinuing Cordarone I.V. In some patients, inserting a pacemaker is required. Despite such measures, bradycardia was progressive and terminal in 1 patient during the controlled trials. Patients with a known predisposition to bradycardia or AV block should betreated with Cordarone I.V. in a setting where a temporary pacemaker is available.

DOSAGE

The dosage for out-of-hospital treament of refractory ventricular fibrillation.tachycardia is 300mg IV push followed by a 10cc NS flush. In the out-of-hospital setting, administer 1.0mg epinephrine (10cc, 1:10000) prior to administering amiodarone.

SUPPLIED

3ml ampules, 50mg/ml

LITERATURE

Weaver, et al. *Circulation* 1990

Harrison, et al. *Annals of Emergency Medicine* 1981

Van Walraven, et al. *Annals of Emergency Medicine* 1998

Kudenchuk, et al. *New England Journal of Medicine* 2000

TESTING
AMIODARONE HCl

1. Amiodarone is given in which of the following doses and routes in the treatment of refractory ventricular tachycardia/fibrillation?

   a. 150mg IV
   b. 300mg IV
   c. 300mg ET
   d. 600mg IV

2. In out-of-hospital use, amiodarone is preceded by what drug and dosage?

   a. Lidocaine, 100-150mg IV
   b. Normal saline, 10cc IV
   c. Epinephrine 1:10,000, 10cc IV
   d. Epinephrine 1:10,000, 10cc IV

3. Immediately after administration of amiodarone, what should be administered?

   a. Normal saline, 10cc IV
   b. Lidocaine, 100-150mg IV
   c. Amiodarone, 300mg IV
   d. Bretylium, 300mg IV

4. Which of the following drugs cannot be administered through the endotracheal tube?

   a. Lidocaine
   b. Amiodarone
   c. Atropine
   d. Naloxone

5. Kudenchuk's paper demonstrated the following about amiodarone and the treatment of ventricular fibrillation cardiac arrest?

   a. Decreased survival compared to bretylium
   b. No change in survival compared to lidocaine
   c. Increased survival to hospital discharge compared to placebo
   d. Increased survival to hospital admission compared to placebo

6. What is amiodarone's most common adverse effect?

   a. Hypotension
   b. Bradycardia
   c. Neonatal hypothyroidism
   d. Cardiac Arrest

7. Amiodarone is incompatible (precipitation occurs) with:

a. D5W
b. Sodium bicarbonate
c. Normal saline
d. Lidocaine

8. Amiodarone may be given how many times in a cardiac arrest patient with refractory ventricular fibrillation?

a. Once
b. Twice
c. As often as needed
d. 150mg IV every 3-5 minutes

9. If amiodarone therapy is unsuccessful, which antiarrhythmic drug is administered next?

a. Bretylium
b. Normal saline
c. Lidocaine
d. Procaineamide

10. Which is the true statement regarding survival from cardiac arrest from refractory ventricular fibrillation?

a. Bretylium results in greater survival than lidocaine
b. Lidocaine does not improve survival
c. Amiodarone when compared with lidocaine improves survival
d. Epinephrine is better than nothing

EMS Protocols

VENTRICULAR FIBRILLATION OR PULSELESS VENTRICULAR TACHYCARDIA

BASIC LIFE SUPPORT:

1. ABC's
2. Assess Airway • High Flow **Oxygen**
3. Perform CPR
4. Transport

ADVANCED LIFE SUPPORT:

1. Place paddles in proper place on the chest of the patient with no pulse and confirm VF/VT

2. If VF/VT confirmed, defibrillate up to 3 times as needed at
   - 200j
   - 300j
   - 360j

3. Start IV **Normal Saline**, intubate, collar and confirm tube placement. Attach Monitor/Defibrillator and continue CPR
   - Initiate fluid bolus of 200-500 cc of **Normal Saline**

4. **Epinephrine** 1 mg IV push, then **Cordarone** 300 mg IV push followed by 10 cc NS flush
   - Hold compressions but continue to ventilate for 15-30 seconds

5. If arrhythmia persists after 30 seconds then defibrillate at 360j

6. If arrhythmia persists, continue CPR, start **Lidocaine** 1.0-1.5 mg/kg IVP.

7. **Epinephrine** 1 mg every 3-5 minute IVP

8. **Magnesium Sulfate** 1-2 grams over 1-2 minutes IVP in refractory VF or Torsades Des Pointes

9. Consider **Sodium Bicarbonate** 1 meg/kg if arrest is unwitnessed or downtime is estimated at greater than 10 minutes

SPECIAL NOTES:

- If **Lidocaine** was given as the initial drug before **Cordarone**, the dose of **Cordarone** should be reduced to 150 mg IVP followed by 10 cc of **NS** flush
- After the first sequence of **Epinephrine** and **Cordarone** together, the procedure should be to administer medication followed by defibrillation after 30-60 seconds with 360j
- In unwitnessed Cardiac Arrest, or prolonged downtime greater than 10 minutes, several cycles of CPR should be performed before defibrillation
- Fluid bolus in Cardiac Arrest has been shown to facilitate perfusion of vital organs
- **Cordarone** may be administered Intraosseously, but not via ETT
- If the patient converts to a viable rhythm anytime during the protocol, start **Lidocaine** 1.0-1.5mg/kg IV push and start **Lidocaine** drip at 2-4 mg/minute

Region VI EMS
Augusta
Georgia

DHR

Frank M. Rumph, M.D., District Health Director

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East Central Health District ◆ 1916 North Leg Road ◆ Augusta, GA 30909-4437 ◆ (706) 667-4326 ◆ FAX (706) 667-4365

Region VI EMS Phone - (706)667-4336 Fax - (706)667-4594

September 3, 1999

MEMORANDUM

TO: EMS Directors
Region VI
Region VI Hospital-ED Dept.
EMS Instructors
Medical Control Physicians

FROM: E. Glenn Bridges, M.D.
On-Line Medical Director, Region VI EMS

RE: Addition of Amiodarone to the Region VI ACLS Protocol for Pulseless Vtach and Vfib

Recent research has indicated a substantial increase in the return of spontaneous pulses when a relatively new antiarrhythmic drug, amiodarone (Cordarone) is added to the standard ACLS protocol for Vfib and pulseless Vtach. All area hospitals and many EMS organizations across the country have added this to their crash carts and drug boxes with good results. The next update of the ACLS guidelines in the year 2000 will undoubtedly include amiodarone. During the interim, the following modifications will be used in Region VI and will become part of the standing orders in our region. When EMS personnel receive the order from Medical Control to "go ahead with ACLS protocol" for these two CPR situations, the following protocol should be carried out if this drug is made available to you by your individual ambulance service director.

-Establish pulseless Vtach or Vfib in a CPR situation.
-Administer up to 3 defibrillation's and reevaluate
-If rhythm is unchanged, establish an airway and IV access and continue CPR.
-Administer epinephrine and 300-mg amiodarone IV push and repeat defibrillation x 3 if needed.
-If rhythm is unchanged, proceed with ACLS as currently done including consideration of Lidocaine, Bretylium, magnesium and sodium bicarbonate with repeated defibrillation's after each intervention.
-A second dose of 150mg of amiodarone IV push should be given 5 minutes after the initial 300mg if needed.

Precautions: Amiodarone (Cordarone) cannot be given per the ET tube
Amiodarone must be flushed from the IV line with a least 10 cc of fluid after its administration. This is most easily accomplished by simply running your IV "wide open" during CPR.
Amiodarone will precipitate if given at the same time as sodium bicarbonate thus making flushing essential when bicarb is given (usually after 10 minutes of "down time").
Early defibrillation remains the single most important treatment of these rhythms and should not be delayed for any reason and should be repeated after every intervention.

Potential side effects include a significant bradycardia after return to spontaneous circulation and this is treated as usual, though external pacing frequently proves most effective.

Loyola University Health System
Chicago, Illinois

VENTRICULAR FIBRILLATION
PULSELESS VENTRICULAR TACHYCARDIA

1. Verify pulselessness

2. **Precordial thump** if arrest is witnessed and defibrillator not immediately available

3. **CPR** until defibrillator available

4. **DEFIBRILLATE** at 200, 300 and 360 WS

   ◊ Do not lift paddles between shocks
   ◊ Visually confirm rhythm between each defibrillation
   ◊ If rhythm converts after defibrillation, proceed to appropriate SOP

5. **Resume CPR** and **INTUBATE. IV ACCESS** as able

6. **EPINEPHRINE** (1:10,000) 1mg IVP and ***AMIODARONE*** 300mg rapid IVP (ONE TIME ONLY)

7. Reassess rhythm within 30-60 seconds

8. If arrhythmia persists or recurs: **DEFIBRILLATE** at 360 WS X 2

9. If arrhythmia persists or recurs: **EPINEPHRINE** (1:10,000) 1mg IVP and **DEFIBRILLATE** at 360 WS X 2

10. If arrhythmia persists or recurs: **LIDOCAINE** 1.5mg/kg IVP or 3mg/kg ET and **DEFIBRILLATE** at 360 WS X 2

11. If arrhythmia persists or recurs: **Repeat LIDOCAINE** 1.5mg/kg IVP or 3mg/kg ET and **DEFIBRILLATE** at 360 WS X 2 in 3-5 minutes if rhythm unchanged

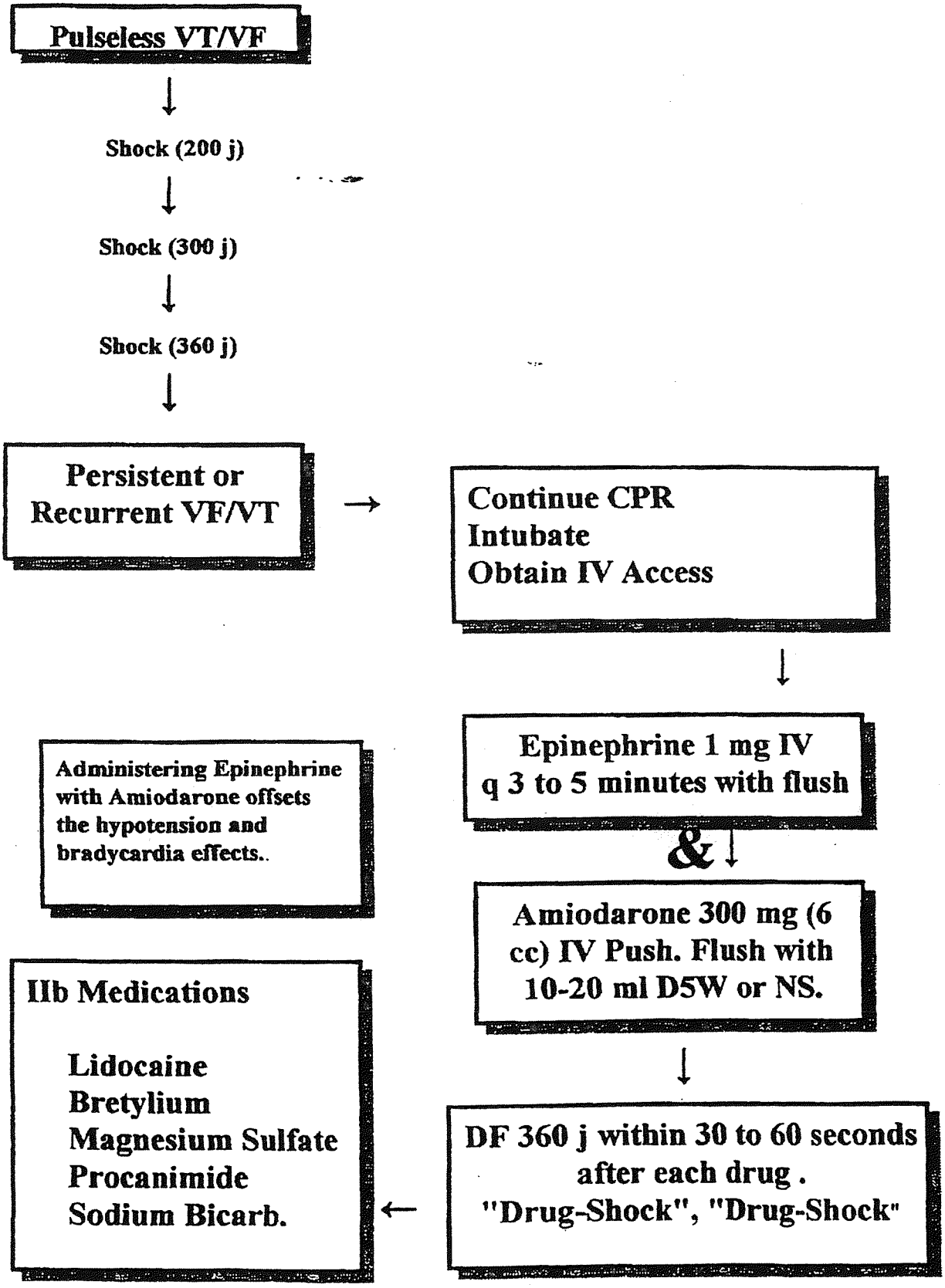
12. Repeat **EPINEPHRINE** (1:10,000) 1mg IVP

13. **DEFIBRILLATE** at 360 WS X 2 after each **EPINEPHRINE** bolus

14. **Continue CPR**

St. Louis EMS
Missouri

Treatment Algorithm for Pulseless Ventricular Tachycardia/Ventricular Fibrillation Utilizing Amiodarone[6]



Nassau County EMS
New York

Protocol for Ventricular Fibrillation/Pulseless V-Tach (Protocol III. B-1) (Paramedic/EMT-CC) (Cordarone IV has been added to this protocol)

Standing Orders:

A. If witnessed perform precordial thump
B. Defibrillate 200 Joules
C. Defibrillate 300 Joules
D. Defibrillate 360 Joules
E. Check pulse and rhythm
F. Intubate, IV Normal Saline or Ringers Lactate
G. Epinephrine 1:10,000 1 mg IV push or ET 2 mg (if no IV) q 3'-5'
H. Defibrillate 360 Joules
I. 2% Lidocaine 1.5 mg/Kg IV bolus or ET 3 mg/Kg (if no IV)
J. Defibrillate 360 Joules
K. Bretylium Tosylate 5.0 mg/Kg IV bolus
L. Defibrillate 360 Joules

IMMEDIATELY FOLLOWING CONVERSION TO AN ADEQUATELY PERFUSING SUPRAVENTRICULAR RHYTHM, ADMINISTER LIDOCAINE 1.5 MG/KG, UNLESS ALREADY ADMINISTERED

Medical Control Options:

A. 2% Lidocaine 0.5 to 0.75 mg/kg IV bolus
B. Epinephrine every 3'-5' (option for escalating and high dose)
C. Bretylium 10 mg/kg IV bolus
D. Sodium Bicarbonate 1mEq/kg
E. Magnesium Sulfate 1-2 gm over 1-2 minutes
F. 0.4 % Lidocaine Drip
G. Dextrose 25 gm, IV bolus
H. Defibrillate 360 Joules
I. Amiodarone IV 150-300 mg IV push

Any of the above orders may be repeated as per physician discretion

3. Protocol Explanations:

- Italics in Standing Orders are only for Paramedics. EMT-CC's must call Medical Control once they finish "H". (EMT-CC's account for the majority of the Nassau County system.)

- Paramedics may proceed further than EMT-CC's before calling in to Medical Control.

- Medical Control Options may be exercised in any order, Options are not listed in priority order. (ie. "I" may be first on a Medical Control MD's list of options before "B", it's the physician's preference).

North Carolina EMS

Ventricular Fibrillation
Pulseless Vent. Tachycardia

UNC HOSPITALS

Orange EMS County

History:	Signs/Symptoms:	Differential:
• Estimated down time • Past medical history/ medications • Events leading to arrest • Renal failure/dialysis • DNR or Living Will	• Unresponsive, apneic, pulseless • Ventricular fibrillation or ventricular tachycardia on ECG	• **Asystole** • **Artifact** • **Device Failure (lead or pad**

Automated Defibrillation Protocol

Cardiac Arrest Protocol

Legend
- **EMT-D and P**
- **EMT-P only**

- **Defibrillate x 3**
  200, 300, 360 joules
- **Continue CPR**
- **IV Protocol**
- **Epinephrine**
- **Amiodarone**
- **Defibrillate 360 joules**
- **Repeat Epinephrine**
- **Defibrillate 360 joules**
- No
- **Criteria for Discontinuation** — Yes → **Stop**
- **Lidocaine**
- **Defibrillate 360 joules**
- **Contact Medical Control** → **Sodium Bicarbonate**, **Calcium Chloride**

Pearls:
- **Exam: ABC's, Mental Status**
- Pattern should be drug-shock, drug-shock, etc. (repeat drugs as per Drug List).
- Reassess endotracheal tube placement frequently and after every move.
- If defibrillation is successful and patient rearrests, return to previously successful energy level.
- Calcium if hyperkalemia is suspected (renal failure, dialysis).
- Defibrillation takes precedence over all treatment once the defibrillator is available.
- If Defibrillation is underway by First Responders (FR), FR defibrillation should continue until 6 defibrillations are accomplished or patient is resuscitated.
- Lidocaine may be substituted for Amiodarone when IV access cannot be obtained.

Disposition:

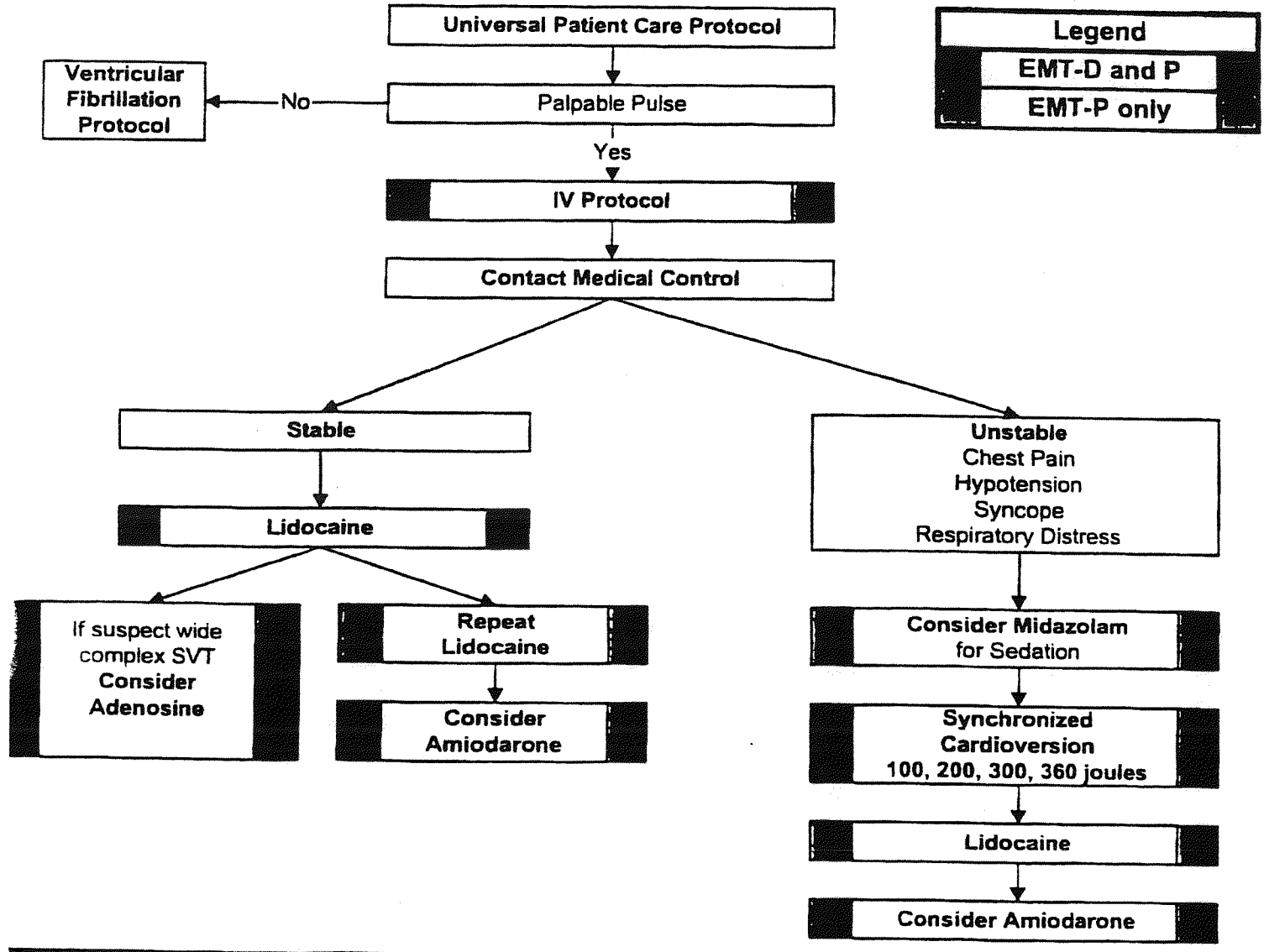
EMS Transport: **ALS:** -Any patient which does not meet the Criteria for Death or Discontinuation of Resuscitation Policies.

Ventricular Tachycardia

History:
- Past medical history/ medications
- Syncope/near syncope
- Palpitations
- Pacemaker

Signs/Symptoms:
- Ventricular tachycardia on EKG
- Conscious, rapid pulse
- Chest pain, shortness of breath
- Dizziness
- Rate usually 150 - 180 bpm

Differential:
- **Asystole**
- **Artifact**
- **Device Failure (lead or pad)**



Pearls:
- **Exam: Vital Signs, Mental Status, Skin, Neck, Lung, Heart, Abdomen, Back, Extremities, Neuro**
- For witnessed/monitored ventricular tachycardia, try having patient cough or deliver a precordial thump.

Disposition:

EMS Transport: **ALS:** -All patients

Oklahoma EMS

PROTOCOL II.11: VENT. FIBRILLATION AND PULSELESS VENT. TACH.

A. Adult Care

I.1. Countershock, 200 J.*

I.2. Countershock, 300 J.*

I.3. Countershock, 360 J.*

I.4. CPR.

I.5. Intubate.

I.6. Epinephrine, 2 mg, If ET tube is clear. Repeat Epinephrine every 3-5 minutes for duration of pulselessness.

I.7. IV, NS, TKO.

I.8. If Epinephrine not yet given via ET tube, give Epinephrine 1.0 mg IV PLUS IV Amiodarone, 300 mg perpheral rapid infusion. NOTE: The 300 mg IV Amiodarone infusion is expected to maintain a reasonable blood level for 20 to 30 minutes, long enough for the patient to be transported to the nearest emergency department.

*I.9. Countershock 360 J**.*

I.10 Lidocaine, 1.5 mg/kg IV or 3.0 mg/kg ET. Repeat Lidocaine 1.5 mg IV in 5 minutes to a total dose of 3.0 mg/kg.*

I.11. Countershock, 360 J.*

** Endotracheal medications should be administered at two times the recommended IV dose. The endotracheal dose should be considered equivalent to the IV dose when calculating the total dose given.*

Consideration for transport should be made at this time.

I.12. Magnesium Sulfate 1 gm IV.

I.13. Countershock, 360 J.*

I.14. Contact Medical Control at earliest opportunity for further orders.

I.15. Consider Sodium Bicarbonate 1.0 mEq/kg, IV.

PROTOCOL II.11: VENT. FIBRILLATION AND PULSELESS VENT. TACH. (cont.)

* If cardioversion restores a supraventricular rhythm with rate 60 and without [illegible] degree A-V block, administer a Lidocaine bolus (if not yet given earlier) 1 mg/kg, IV, and start Lidocaine drip at 2 mg/min. (adult).

B. Pediatric Care

I.1. Countershock 2 J/kg*.

I.2. Countershock 4 J/kg*.

I.3. Countershock 4 J/kg*.

I.4. CPR.

I.5. Intubate.

I.6. Epinephrine 1:1,000, 0.1 mg/kg (0.1 ml/kg) ET if ET route is clear.

I.7. IV, NS, TKO.

I.8. Establish intraosseous access if unsuccessful after 2 IV attempts or 2 minutes in child less than 6 years.

I.9. If Epinephrine not yet given via ET tube, give first dose IV or IO, 1:10,000, 0.01 mg/kg (0.1 ml/kg).

I.10. Countershock 4 J/kg**.

I.11. Lidocaine 1 mg/kg, IV or IO or 2 mg/kg ET may be repeated once in 5 minutes.

I.12. Countershock 4 J/kg**.

I.13 Epinephrine, second and subsequent doses, 1:1,000 0.1 mg/kg (0.1 ml/kg) IV/IO or ET. Repeat every 3-5 minutes.

I.14. Countershock 4 J/kg**.

I.15. Countershock 4 J/kg**.

PROTOCOL II.11: VENT. FIBRILLATION AND PULSELESS VENT. TACH. (cont.)

I.16. Countershock 4 J/kg**.

I.17. Contact Medical Control at earliest opportunity.

I.18 Consider Sodium Bicarbonate 1.0 mEq/kg, IV or IO.

II.1. None.

* If cardioversion restores a supraventricular rhythm with rate 60 and without 2nd or 3rd degree A-V block, administer a Lidocaine bolus (if not yet given earlier) 1 mg/kg, IV, and start Lidocaine drip, 20-50 mcg/kg/min (pediatric).

** Defibrillations should be performed 30-60 seconds after drug delivery. The pattern should be drug-shock-drug-shock. If delays occur because of medication administration or the performance of procedures, go back to defibrillate before proceeding.

EMT-D Transition to Advanced Life Support Care

In accordance with the American Heart Association Advanced Cardiac Life Support Guidelines, paramedics arriving at the scene of a patient with a Semi-Automatic Defibrillator in place should attach a conventional defibrillator when clinically convenient. If a Semi-Automatic Defibrillator is in the process of analyzing, the paramedic should allow the analysis to be completed and a shock delivered, if advised. Once the shock has been delivered or "No Shock" is advised, the patient should then be switched to a conventional defibrillator in order to avoid time delays associated with semi-automatic analysis and defibrillation.

Montgomery County EMS
Texas

Ventricular Fibrillation
Adult

Montgomery County Hospital District
Standing Delegated Orders

Patient Criteria:

Pulseless
Apneic
ECG: V- Fib or Pulseless V-Tach

Required Assessment:

CABC's
ECG
Blood Glucose
- BGL <80 refer to Hypoglycemia SDO

Required Interventions:

- **CPR**
  - BVM with 100% O_2
- **"Stacked" Defibrillation's** as rapidly as possible unless VF converts
  - **200j**
  - **300j**
  - **360j**
- **Intubate**
- **IV .9%NaCl**
- **Epinephrine 1:10,000 1.0 mg IVP or 2.0 mg ET**
  - Administer via first available route
- **Lidocaine 1.5 mg/kg IVP or 3.0 mg/kg ET**
  - May repeat x 1
- **Defibrillate @ 360j or 3 "Stacked" Defibrillation's at 360j**
  - Defibrillation should be within 30 – 60 sec after medication
- **Epinephrine 1:10,000 1 mg IVP or 2 mg ET**
- **Cordarone 150 mg IVP**
  - Flush with 20 ml NACL
- **Epinephrine: Escalating**
  - 1 mg-3 mg-5 mg IVP
  - Repeat q 3-5 minutes- subsequent dosing should be 5 mg
- **Cordarone 150 mg IVP**
  - Flush with 20 ml NACL
- **Magnesium Sulfate 1.0-2.0 gm <u>slow</u> IVP**
  - For refractory v-fib or Torsades des Pointes

Intervention Options:

- **Nasogastric Tube**
  - #18 Salem Sump
- **Blood Glucose**
  - BGL <80 refer to Hypoglycemia SDO
- Any changes in condition or rhythm refer to appropriate SDO

Consult Only:

- **Sodium Bicarb 1 meq/kg**
  - If acidosis suspected
- **Narcan 2.0mg – 8.0mg IVP**
  - For suspected drug/narcotic overdose
- **Ca Gluconate 500 mg- 1 gm IVP**
  - **For Renal Dialysis Patients only**

Ventricular Tachycardia-Unstable Wide Complex-Adult

Montgomery County Hospital District
Standing Delegated Orders

Patient Criteria:

Chest Pain with:
- Dizziness
- Confusion
- Weakness

Systolic B/P < 90mmHg **And** one or more of the following:
- Severe Dyspnea
- Severe pulmonary edema
- Significant altered mentation

ECG: Wide Complex Ventricular Tachycardia (QRS > .12 seconds)

Assessment:

CABC's

Vital Signs

Pulse Oximeter

ECG
- 12-Lead if able to accomplish without interfering with treatment

Required Interventions:
- **O_2 100%**
- **IV .9%NaCl**
- **Lidocaine or Cordarone**
  - As outlined in options

Intervention Options:
- **Lidocaine 1.0 mg/kg IVP**
  - Q 5min as 0.5mg/kg up to 3.0mg/kg total
- **Lidocaine infusion 2-4 mg/min**
  - If successful conversion of the rhythm with Lidocaine bolus
- **Cordarone 150 mg IV Bolus**
  - Flush with 20 ml NACL
  - May repeat once
- **Cordarone infusion 1 mg/min IV**
  - If successful conversion of the rhythm with Cordarone bolus
- Any changes in condition/rhythm refer to appropriate SDO
- **Synchronized cardioversion 100J**
- **Synchronized cardioversion 200J**
- **Synchronized cardioversion 300J**
- **Synchronized cardioversion 360J**

Consult Only:

- **Diazepam 2.0-10.0 mg IVP**
  - for sedation for cardioversion
- **Repeat Cardioversion 360 J**

Ventricular Tachycardia-Stable Wide Complex-Adult

Montgomery County Hospital District
Standing Delegated Orders

Patient Criteria:

ECG: Ventricular Tachycardia-Wide Complex (QRS > .12 seconds)
- Systolic BP>90 mmHg

Without significant
- Dyspnea / SOB
- Pulmonary edema
- Altered mental status

Assessment:

CABC's

Vital Signs

Pulse Oximeter

ECG
- 12-Lead if able to accomplish without interfering with care

Required Interventions:
- **O_2 100%**
- **IV .9%NaCl**
- **Lidocaine or Cordarone**
  - As outlined in options

Intervention Options:
- **Lidocaine 1.0 mg/kg IVP**
  - Q 5min as 0.5mg/kg up to 3.0mg/kg total
- **Lidocaine infusion 2-4 mg/min**
  - If successful conversion of the rhythm with Lidocaine bolus
- **Cordarone 150 mg IV over 10 min.**
  - May repeat once
- **Cordarone infusion 1 mg/min**
  - If successful conversion of the rhythm with Cordarone bolus
- Any changes in condition/rhythm refer to appropriate SDO

Consult Only:
- **Diazepam 2.0-10.0 mg**
  - Sedation for cardioversion
- **Synchronized cardioversion 100J**
- **Synchronized cardioversion 200J**
- **Synchronized cardioversion 300J**
- **Synchronized cardioversion 360J**

Ventricular Ectopy

Montgomery County Hospital District

Non-Sustained Ventricular Tachycardia Adult

Standing Delegated Orders

Patient Criteria:

Chest pain with:
- Weakness
- Dizziness
- SOB
- Irregular heart beat

ECG:
- Premature Ventricular Complexes > 6/min for more than 5 min.
- Evidence of acute myocardial ischemia and/or myocardial Infarction
- In the absence of Bradycardia

Assessment:

CABC's
Vital Signs
Pulse Oximeter
ECG

Required Interventions:

- **O_2 100% ASAP**
- **IV .9%NaCl**
- **Lidocaine 1.0 mg/kg IVP**

Intervention Options:

- **Additional Lidocaine 0.5 mg/kg IVP**
  - if ectopy not resolved q 5 min up to 3.0 mg/kg
- **Lidocaine Infusion 2-4 mg/min**
  - If successful conversion of the rhythm with Lidocaine bolus
  - Any changes in condition/rhythm refer to appropriate SDO
- **Cordarone 150 mg IV over 10 min.**
  - May repeat x 1
- **Cordarone infusion 1 mg/min IV**
  - If successful conversion of the rhythm with Cordarone bolus

Consult Only:

- **Magnesium Sulfate 1.0 gm-2.0 gm IVP**
  - For Torsades de Pointes

Post-Resuscitation Management
Adult

Montgomery County Hospital District
Standing Delegated Orders

Patient Criteria:	Patient with spontaneous circulation (palpable carotid/radial pulse) after being treated for any non-perfusing rhythm
Assessment:	CABC's Vital signs Pulse Oximeter Reassess ET if applicable
Required Interventions:	• **O_2 100%** ▫ BVM / Intubation as needed • **IV .9%NaCl**

Intervention Options:	• **Lidocaine 1.0 mg/kg IVP**
	  ▫ if converted from a ventricular rhythm and **NOT** bradycardic
	• **Lidocaine Infusion 2-4 mg/min**
	• **Cordarone 150 mg IV over 10 min.**
	  ▫ May repeat once
	• **Cordarone Infusion 1mg/min IV**
	  ▫ If converted from a ventricular rhythm after administration of Cordarone and not bradycardic or hypotensive
	• **Dopamine Infusion 5-20 mcg/kg/min IVP**
	  ▫ if still hypotensive 5 minutes after conversion from any rhythm **except** PEA which becomes perfusing after a fluid bolus
	• **If Bradycardia, Use Bradycardia SDO**
	• **Blood Glucose**
	  • BGL <80 refer to Hypoglycemia SDO

Consult Only:	

Rural Metro Medical Services
North Texas Division

Rural/Metro Medical Services

Protocols for Treatment

North Texas Division

Robert Genzel, MD

Ventricular Fibrillation/Pulseless Ventricular Tachycardia

1) Defibrillate at escalating levels 200J, 300J, 360J. Check rhythm and pulse between shocks. If at any time the rhythm changes go to the appropriate protocol. For patients remaining in VF/Pulseless VT:
2) Begin CPR
3) Intubate and establish IV .9NS KVO.
4) Administer Epi 1:10,000 1mg IVP or 2.5 mg via Ett repeat using escalating dosing (2mg, 5mg, 10mg) at 3-5
5) Continue CPR and allow medications to circulate for 1 minute.
6) If still in VF/VT defibrillate at 360J.
7) If patient remains in VF/VT proceed immediately to #8.
8) Administer Lidocaine 1.5 mg/kg IVP and defibrillate after 1 minute of CPR.
9) If patient remains in VF/VT administers Cordarone 150 mg IVP and defibrillate after 1minute of CPR
10) If patient remains in VF/VT check Ett placement and administer Lidocaine 1.5mg/kg, Cordarone 150 mg IVP and defibrillate after 1 minute of CPR.
11) If patient remains in VF/VT administer Mg 2g IVP and defibrillate after 1 minute of CPR.
12) If patient remains in VF/VT administer Bretylium 5mg/kg IVP and defibrillate after 1 minute of CPR.
13) Initiate transportation and contact BSP for further orders.
14) Continue to defibrillate every 2-3 minutes if patient remains in VF/VT, and give Bretylium 10mg/kg IVP 8-10 minutes after the initial Bretylium dose.

Ventricular Tachycardia (with a pulse)

Stable V-Tach (Normal mental status, normotensive, no severe dyspnea or chest pain)

1) Administer O2 by NRBM
2) Establish IV NS
3) Lidocaine 1.5 mg/kg IVP (If Torsades de pointes start with Mg 2g IVP & Do Not use Cordarone)
4) If no change in rhythm in 2-3 minutes administer Lidocaine 1.5 mg/kg IVP
5) If no change in 2-3 minutes administer Mg 2g IVP over 10 minutes
6) If no change in 2-3 minutes consider alternative diagnosis such as SVT with aberrancy, S.Tach with bundle branch block.
7) When rhythm converts begin Lidocaine drip at 2-4 mg/min.
8) Initiate transportation and contact BSP.

Unstable V-Tach (Altered mental status, hypotension [SBP<90], severe dyspnea or chest pain)

1) Administer O2 by NRBM
2) Establish IV NS
3) Contact BSP for synchronized cardioversion, if patient is conscious administer **Valium 5mg to 10 mg IVP**
4) Cardiovert at 50J, escalating 75J, 100J, 200J, 300J, 360J until conversion occurs.
5) Once conversion occurs, or if V-Tach recurrent after initial successful cardioversion administer Lidocaine 1.5 mg/kg IVP, may repeat Lidocaine 1.5 mg/kg IVP if V-Tach or frequent PVC's recur.
6) Begin Lidocaine drip at 2-4 mg/min.
7) If V-Tach persistent administer Cordarone 150 mg IVP may repeat x1 if V-Tach continues.(Do Not use Cordarone in Torsades de Pointes, Use Mg 2g IVP instead)
8) Initiate transportation and contact BSP.
9) Consider Bretylium 5mg/kg or Mg 2g IVP if Lidocaine/Cordarone not effective)

VENTRICULAR FIBRILLATION (VF)

DEFINITION: Patients who are apneic and pulseless with ventricular fibrillation or ventricular tachycardia.

TREATMENT

1. CPR - only until defibrillator is attached
2. Defibrillate up to 3 times if needed for persistent VF/VT
3. CPR
4. Intubate/Ventilate 100% oxygen/monitor lead II ECG/IV NS
5. Epinephrine 1 mg IVP
   ~~Amiodarone~~ 300mg IVP
6. Defibrillate 360 joules if needed for persistent VF/VT
7. **CONTACT BIOTEL (after 1st round of drugs administered)**
8. TREATMENT CONSIDERATIONS:
   a. Defibrillation
   b. Epinephrine

Standard Dose:	1mg IVP	Repeat q 3-5 minutes
Intermediate Dose:	2mg - 5 mg IVP	Repeat q 3-5 minutes
Escalating Dose:	1mg-3mg-5mg IVP	3 minutes apart
High Dose:	0.1mg/kg IVP	Repeat q 3-5 minutes

   c. Lidocaine 1.5mg/kg IVP
   d. Bretylium 5mg/kg IVP; Repeat 10mg/kg IVP
   e. Magnesium Sulfate (10%) 1gm-4gm SLOW IVP
   f. Calcium Chloride (10%) 10mg/kg - 15mg/kg SLOW IVP
   g. Sodium Bicarbonate (NaHCO3) 1meq/kg IVP
   NOTE: Items h, i, j and k may be considered in the post resuscitation phase
   h. Lidocaine drip 1-4 mg/minute
   i. Bretylium drip 1-4 mg/minute
   j. Dopamine drip 2-10 mcg/kg/minute (refer to chart page 31 for drops/minute)
   k. Levophed drip 8-12 mcg/minute (refer to chart page 31 for drops/minute)

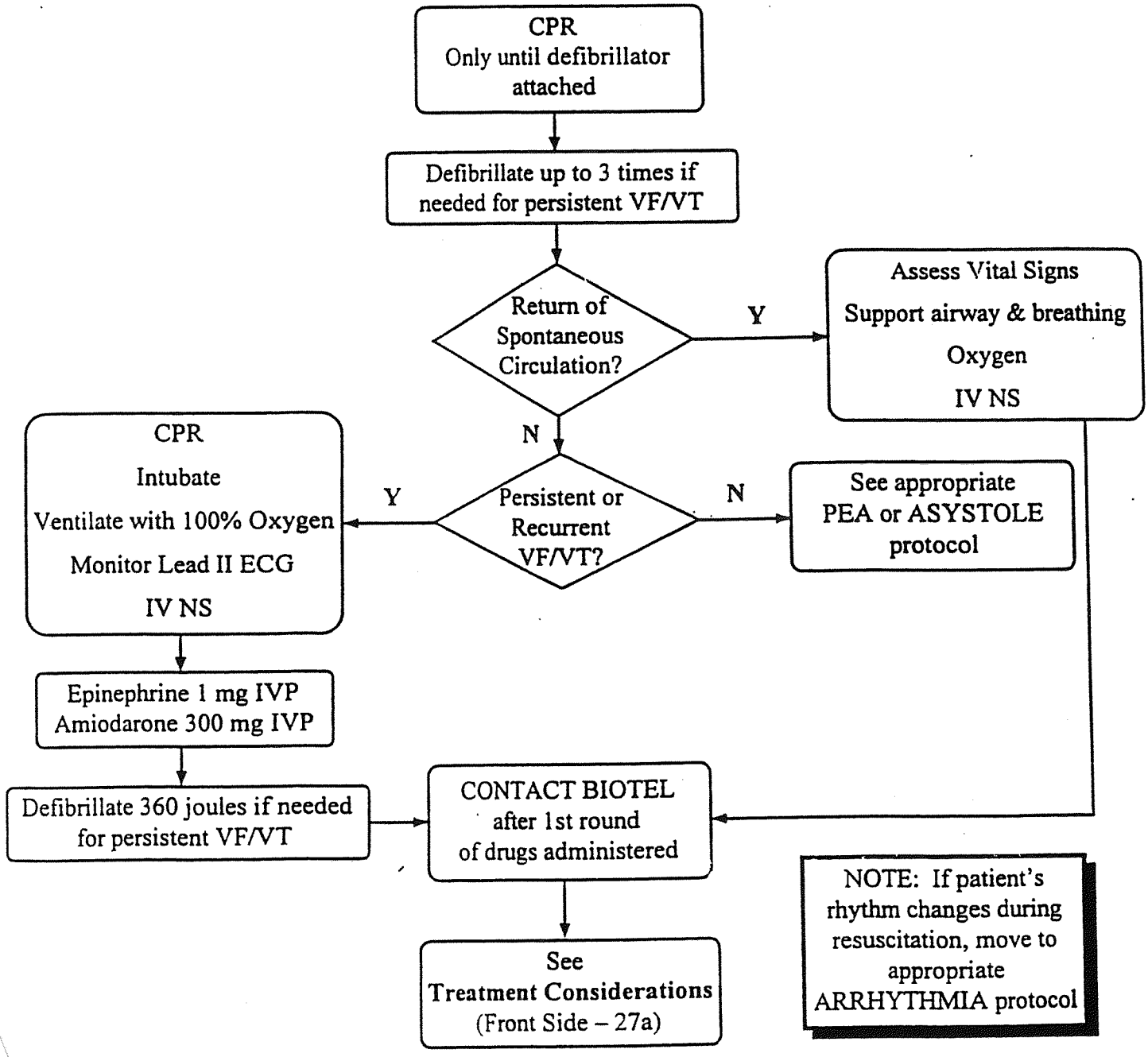
PEDIATRIC

VF is a very unusual presentation in pediatrics
Defibrillation 2 joules/kg; repeat 4 joules/kg
Epinephrine 1st dose (1:10,000) 0.01 mg/kg IVP; Subsequent doses (1:1,000) 0.1 mg/kg IVP
Lidocaine 1mg/kg IVP

NOTE: If patient's rhythm changes at any time during resuscitation, refer to appropriate protocol.

VENTRICULAR FIBRILLATION (VF)

DEFINITION: Patients who are apneic and pulseless with Ventricular Fibrillation or Ventricular Tachycardia.



PEDIATRIC PATIENTS:

VF is a very unusual presentation in pediatrics.
Defib at 2 joules/kg; Repeat at 4 joules/kg
Epinephrine 1st dose (1:10,000) 0.01mg/kg IVP; Subsequent doses (1:1,000) 0.1mg/kg IVP
Lidocaine 1mg/kg IVP